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Electroorganic synthesis:

Inter- and Intra-molecular Anion Radical Cycloadditions, and

Electrogenerated Base promoted coupling reactions

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Electroorganic synthesis:

Inter- and Intra-molecular Anion Radical Cycloadditions, and

Electrogenerated Base promoted coupling reactions

By

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Dissertation

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Lives of great men all remind us

We can make our lives sublime

And, departing, leave behind us

Footprints on the sands of time

H. W. Longfellow

Dedication

This thesis is dedicated to my wife, whose support and encouragement has sustained me, and whose life I am so lucky to share in, thank you, my Tara.

Acknowledgements

I would like to whole heartedly thank Professor Nathan L. Bauld for his guidance and unfettered support, for taking on that one last graduate student. It has, quite simply, been an *honour* to work with you.

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Thank you also to my mother, brother, sister, brother-in-law and niece (Shelagh, Scott, Claudia, Glenn, and Francesca). Thanks to Gary and Rob, for their ability to raise conversation to an artform.

This thesis is also in memoriam for my father, George, whose sage council and love is always missed. I wish you could have seen this.

Electroorganic synthesis:

Inter- and Intra-molecular Anion Radical Cycloaddition, and

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The University of Texas at Austin, 2005

Supervisor: Nathan L. Bauld

The electrochemical promotion of a variety of organic synthetic procedures has been investigated. These procedures are seen to fall into two categories, those promoted by anion radicals, and those promoted by electrogenerated base.

The intramolecular anion radical cyclization of bis(enones) leads to the formation of both cyclobutane and Diels-Alder cyclic products. The formation of these products is shown to occur via a distonic anion radical intermediate. The majority of reactions are seen to be mildly electrocatalytic, indicating an electron transfer chain. The primary use of tetraethylammonium tetrafluoroborate as the electrolyte leads to high pericyclic yields, and is therefore presented as an effective synthetic route. Synthetic and mechanistic considerations are widely explored, particularly via systematic substrate alteration.

Additionally, variation of the perchlorate electrolyte cation is seen to lead to dramatic diastereoselectivity, indicative of electrolyte chelation with the distonic anion

radical. Indeed this work is the first to synthetically utilize Barium perchlorate electrolyte.

Intermolecular anion radical cross-cyclobutanation reactions are shown to yield novel compounds, albeit in moderate yield. The cross reactions are generally based upon the previously known anion radical cyclobutanating reactivity of phenyl vinyl sulfone. The reactivity of ketones, with sulfones, is only the third example of intermolecular anion radical cyclobutanation.

The Electrogenerated Base (EGB) promoted additions of allyl phenyl sulfone to electron deficient alkenes was studied. This carbanion based chemistry leads to Michael additions, primarily yielding two classes of product, that of single addition and of double addition. Addition to vinyl sulfones approached quantitative yields, giving exclusive 1:2 (double addition) product formation, and electrocatalytic factors of greater than 10. Addition to a variety of other electron deficient alkenes gave a mixture of 1:2 and 1:1 adducts and in some cases, secondary reaction products. Although formed in moderate yield, the formation of an eight member ring from the α,γ-addition of the allyl phenyl sulfone carbanion to divinyl sulfone is quite remarkable.

Further EGB research is briefly explored. Firstly, use of a pro-base (in some cases the *in situ* substrate) to give reactive cyanomethyl anions. Leading to near quantitative yields of acyclic cyano sulfones, produced with electrocatalytic factors greater than 30. Secondly, use of a pro-base, namely diphenyl sulfone, to increase EGB reaction efficiency and promote carbanion mechanism addition reactions of allyl/propenyl species. Lastly, the use of EGB's to promote electro-isomerization is observed.

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CHAPTER I: Electroorganic synthesis

The use of electrochemistry (EC) to promote organic synthesis has a long history stretching back to the decarboxylate dimerization Kolbe reaction in the mid-19th century.[1] Electroorganic chemistry then advanced onward into the 20th century with increased study of organic electrode processes, by investigators such as Tafel and Haber.[2] While much of this early work delt with aqueous electrolyte solutions, it was not until the mid-20th century that research turned toward non-aqueous systems. Indeed, the discovery of the quantitative Baizer-Monsanto[3] hydrodimerization process (adiponitrile from acrylonitrile) led to a resurgance of interest in electroorganic synthesis. The industrial scale up of which makes for an extremely profitable sythetic route to the Nylon precursor. Recent decades have seen the publication of a wide variety of carbon-carbon bond formation/cleavage reations, all promoted by electrochemistry.[4] Electrochemical synthetic approachs are seen in a variety of other industrial applications: Oxidative formation of gluconic acid; Hydrogenation formation of piperidine; Halogenation to give perfluoro acids; even organometallation to give tetra-ethyl lead.[5]

However, the use of EC as a synthetic tool is still overlooked, with little coverage in general organic chemistry texts. Such coverage rarely extends beyond the Kolbe reaction, and even more detailed texts devote a handful of pages to EC techniques (for example, apx. 4 out of 1300).[6] This lack of penetration, in my opinion, has two primary and linked causes. The negative feedback can be considered to begin with dogmatic methodology and nomenclature, providing a rather higher barrier to the uninitated. This of course leads to limited use of EC in synthesis, such that there are few good examples

of synthetic EC, and so that researchers do not feel any need to fight their way through EC methodology. It is interesting to note that on one occasion a referee for one of my organic synthesis papers, asked for more EC methodology to be included, such as cyclic voltammetry data. Yet, the same referee asked for an expanded introduction to help explain EC techniques to a general organic audience. It is the contention of this thesis, that this work is synthetic chemistry utilizing EC methods. The thesis shows that EC can be used without a vast methodological underpinning to achieve synthesis. The use of cyclic voltammograms in this work is therefore limited, so that a general organic reader may consider this approach synthetically viable.

Electrochemical mechanistic studies are entirely useful and interesting approaches to finding ways to improve upon a given electroorganic preparation. However, this is an area that will only briefly be touched upon. Rather this work was directed at a wide range of synthetic targets, instead of utilizing EC to get complete mechanistic information. Indeed, such information on just one reaction class could easily amount to a thesis in itself, for example the first published intermolcular anion cyclization paper appeared in 1990,[7] yet was not mechanistically investigated until 2004.[8]

An electrochemical reaction involves the transfer of electrons between an electrode and a molecule of substrate. This thesis deals exclusively with reductive approaches, where the working electrode is an electron source, and therefore the cathode. This work revolves around a three electrode divided cell, cathode (Working Electrode: WE), anode (Counter Electrode: CE) and Reference Electrode (RE), to measure and control the potential across the solution. The main compartment of the cell contains the WE, with the RE placed nearby, while another compartment (divided by a frit) contains

the CE (shown in Figure I-1). The solution throughout is non-aqueous (usually acetonitrile), along with an added electrolyte. Charge moves through this ionized salt solution via migration of ions, either of the electrolyte or of the substrate.

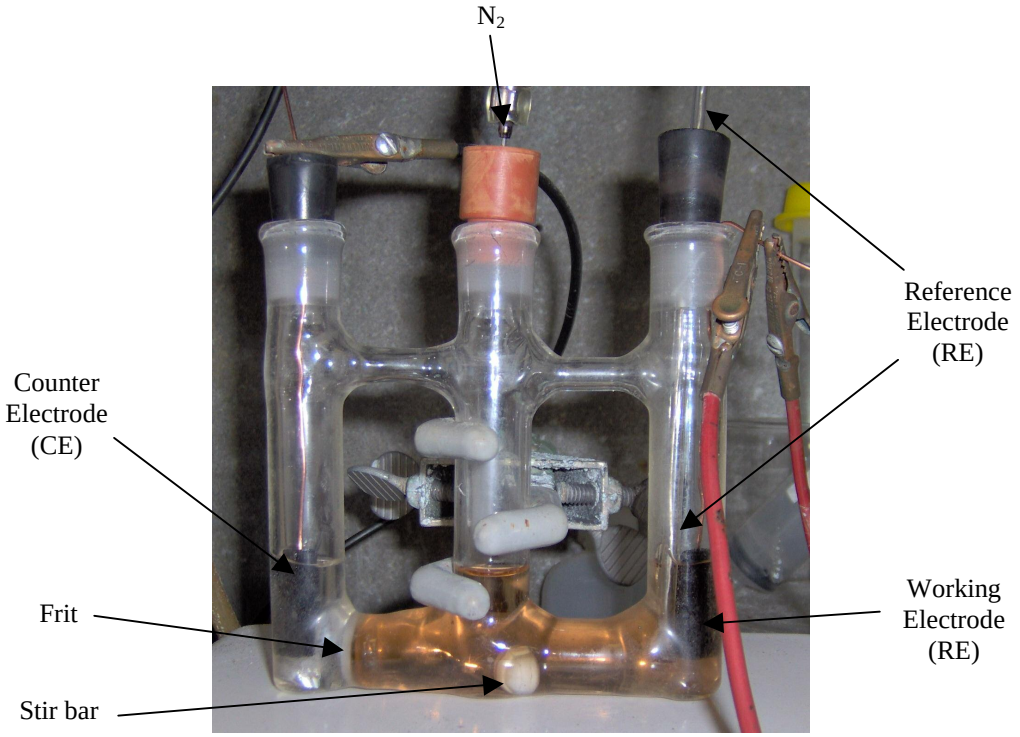

Figure I-1. Anotated picture of divided electrochemical cell (post electrolysis).

A coulometer is placed in series to record the amount of charge (in Coulombs) that has flowed through the cell in a given electrolysis (reaction run). The amount of charge used is related to the electrocatalytic nature of the reaction being studied. A catalytic factor will be quoted for reactions throughout this thesis, based upon total charge used and moles of limiting reagent consumed. Catalytic factors are found using 96485 C mol^{-1}, a number derived from the product of the Avogadro constant and the elementary charge on an electron.[9] This number is also refered to as a Faraday (F), such

that a reaction that gave one mole of product for every mole of charge would be a 1.0 F process, and would not be catalytic. However, a 0.1 F process would have a catalytic factor of 10, as ten moles of product are produced for each mole of charge. The reactions were monitored for completion in a step-wise fashion, such that the exact amount of charge used to give completion is not known (see experimental data). Therefore, the catalytic factors may be greater than that stated, and is subsequantly refered to as a minimum catalytic factor.

The electrochemical approach employed in this thesis has a number of advantages over both traditional organic synthesis and other electrochemical approaches. Firstly, the advantages over traditional organic synthesis primarily arise from the use of electricity as the sole reagent. This simplification allows for enhancements in cost-effectiveness by utilising no reagent, limiting reaction complexity, and the lack of waste chemicals (electrolytes, such as poisonous perchlorates, are feasibly re-usable components). Secondly, by avoiding the common electrochemical approach of using a mercury pool electrode, further simplification advantages are gained. These two features allow the "green" chemistry label to be advanced for this electrochemical approach. The key advantage of this electroorganic synthetic approach is the access to a variety of entirely novel compounds, in what are effectively single step electrocatalytic reactions in high yield.

This thesis deals with several areas of electroorganic chemistry, and each will be fully introduced in a separate chapter. Broadly, the thesis is divided into two portions, initially looking at anion radical promoted reactions, of both inter- and intramolecular nature, and then moving onto Electrogenerated Base (EGB) chemistry. There is a degree

of interplay between these two mechanistic pathways throughout this research. A variety of attempts to select a particular pathway are advanced to improve the yield of the desired product. Research upon the intramolecular anion radical cyclization of bis(enones) will be presented in chapters two and three. Chapter two looks at the myriad mechanistic and scope implications of variations in the structure of said bis(enones), while advancing a synthetically viable electrolyte/solvent system, that of tetraalkylammonium tetrafluroborate/acetonitrile, which gives "pericyclic" yields approaching 90%. It should be noted that the terms pericyclic and Diels-Alder are used throughout this work in an overall reaction sense. Rather than in the strictly mechanistic sense, of the concerted reactions generally referred to by these terms.

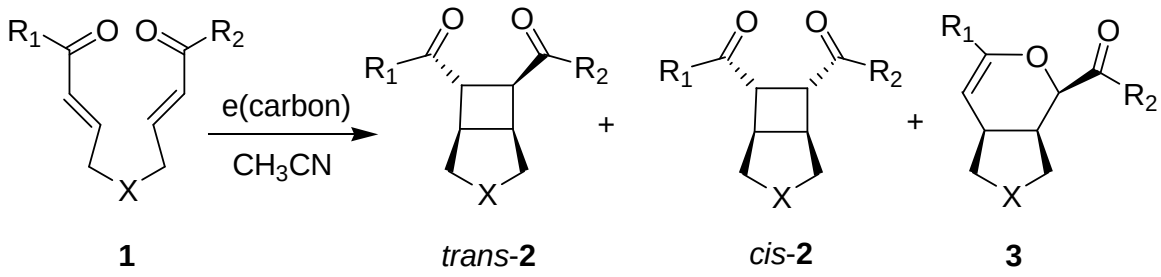

Figure I-2. Pericyclic products in the electrocatalytic, intramolecular anion radical cyclobutanation reactions of various bis(enones).

Chapter three probes the dramatic effects of electrolyte variation on product diastereoselectivity in these bis(enones). The use of varied metal perchlorate electrolytes is seen to effect the ratio of pericyclic products formed, via a transition state intercalation of the metal anion.

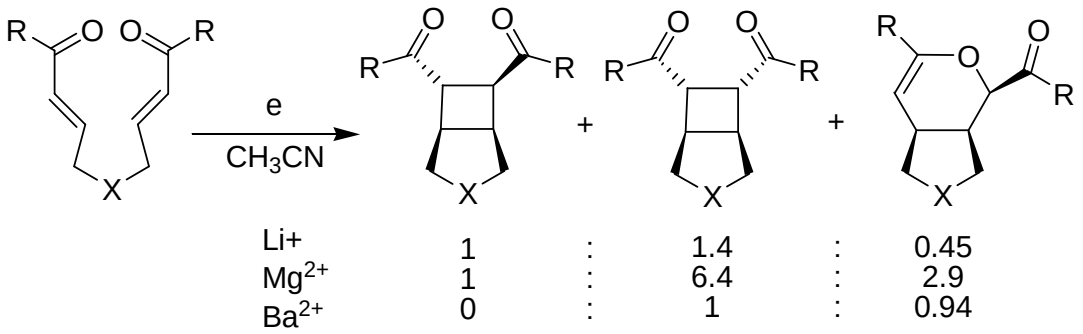

Figure I-3. The effect of varying perchlorate electrolyte on the ratios of pericyclic products formed in the electrocatalytic, intramolecular anion radical cyclization reactions of several bis(enones).

The somewhat less successful intermolecular anion radical cyclizations of several vinyl sulfones and ketones are presented in chapter four. The yields observed, while approaching 50%, appear to be depressed by the competing EGB pathways, and subsequent products, along with unspecified polymerization processes.

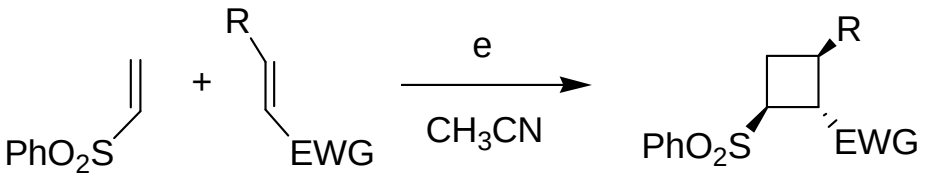

Figure I-4. Reactants involved in the cross-electrocyclobutanation reactions.

Chapter five moves into Electrogenerated Base (EGB) promoted addition reactions of allyl phenyl sulfone to electron deficient alkenes. Where a dichotomy of products is seen, namely between 1:1 “dimeric” addition products, formed in modest yields and 1:2 “trimeric” products formed in very good yield.

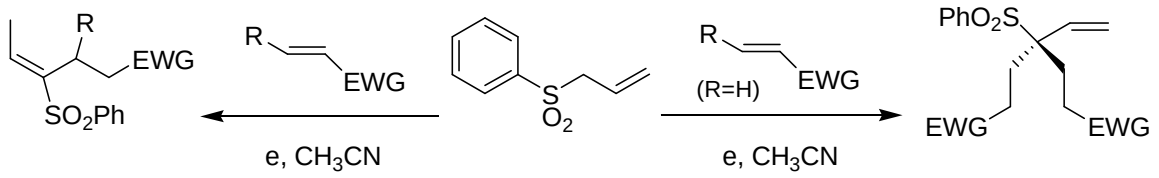

Figure I-5. The electroreduction of allyl phenyl sulfone leads to the formation of a carbanion which undergoes Michael addition to a variety of vinyl compounds (containing Electron Withdrawing Groups), generally giving two classes of product.

Chapter six turns to a number of underdeveloped synthetic EGB related threads. These include cyanomethyl anion addition reactions, where cyanomethylation is seen to occur extremely readily for a small number of compounds, which act as their own EGB, and to a lesser extent when an added pro-base is needed. The addition of pro-base improves the yield of allyl phenyl sulfone carbanion addition reactions, and initiates similar reactions in other allyl/propenyl compounds. The use of EGB's to promote allyl to propenyl isomerization. Finally, added weak acids trap EGB reaction intermediates.

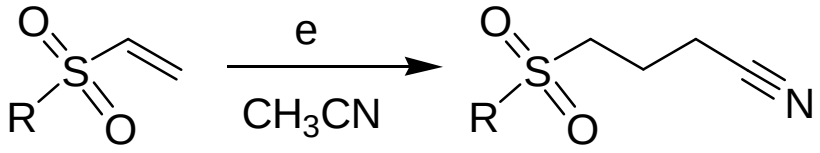

Figure I-6. The electroreduction of alkyl vinyl sulfones leads to the formation of a reactive cyanomethyl carbanion, which undergoes Michael addition, to the vinyl sulfone substrate.

The thesis is then rounded out with an experimental section, which includes details of each experiment reported/discussed in the chapters, along with characterizations. In general characterizations are more detailed for chapters two, three and five, and less detailed for chapters four and six. The large quantity of unsuccesful reactions are not detailed, except for the handful of occasions where a direct comparison to a succesful alternate procedure is made in the text of the corresponding chapter.

The substrate and product numbering system is designed to be consistent throughout this thesis, despite the slight complication of the same substrate being used in different chapters for both anion radical and EGB experiments. This does lead to apparent numbering discrepancies on occasion. While a handful of substrates are encountered first in chapter IV, they can more easily be considered part of a suite of substrates utilized in chapter V, such that there is no ideal way to number these substrates. Numbering based upon chapter V has been employed, so that the larger number of substrates (21) are presented there in a systematic and logical manner. This does impinge somewhat on the numbering logic of chapter IV, where six of these substrates are first encountered.

Additional conventions are also employed, such that all cyclobutanes are numbered as product **2**. When formed via intramolecular cyclization of a bis(enones) the number is followed by a single letter, while formation via intermolecular cyclization gives products where the number is followed by two letters, referencing the constituent substrates (see chapter four). Similarly, all trimeric products formed from the sequential addition of a carbanion to two moles of a different substrate are numbered **11**. When this carbanion is formed from allyl phenyl sulfone, then a single letter references the

constituent substrate (see chapter five), while carbanion's of other molecules will give trimeric products with three letters after the number, referencing all constituent substrates, the first letter being the carbanion source (see chapters four and six). All product structures are given in the experimental section alongside characterization information.

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CHAPTER II

Intramolecular anion radical cyclization of bis(enones)

II-1. Introduction

Cyclobutanation reactions of the cation radicals of alkenes with neutral alkenes have by now become rather commonplace and are characterized by impressively high cycloaddition rates and low activation barriers, especially in comparison to the corresponding thermal reactions.[1,2] There have been some recent indications that this extensive body of cation radical cyclobutanation chemistry may have a close counterpart in the domain of anion radical chemistry. Specifically, the reduction of phenyl vinyl sulfone under electrochemical conditions (mercury pool cathode) has been reported to yield *trans*-1,2-bis(phenylsulfonyl)cyclobutane.[3] Subsequently, the cyclodimerizations of a variety vinylpyridines and vinylquinolines under similar conditions have also been established.[4] Still more recently, a few intramolecular anion radical cyclobutanations of tethered bis(enones) have been described from these laboratories.[5,6] These anion radical reactions are of special interest because they represent rare examples of intramolecular anion radical cycloaddition, rather than the more common electrohydrocyclization/dimerization (EHC or EHD).[7,8]

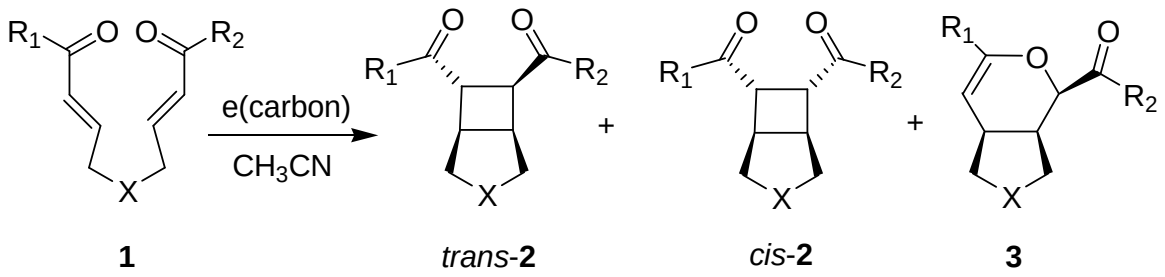
The environmentally benign nature of these electrochemical conversions, inherent in the simplified workup and the consumption of electricity as the sole reagent (in catalytic amounts), further add to their experimental appeal and potential utility. This chapter reports the development of substantially more efficient conditions than those previously reported for carrying out these electrocatalytic intramolecular cycloaddition

reactions in high yields, and further extends the scope and defines the limitations of these reactions. In particular, the use of tetraalkylammonium tetrafluoroborates as electrolytes in acetonitrile solution is developed as a particularly efficient method for these cyclobutanations. From a mechanistic viewpoint, experiments are described which strongly support the formulation of the cycloaddition reaction as proceeding in a stepwise fashion, *via* a distonic anion radical intermediate. Other new mechanistic and theoretical aspects of the reaction are clarified, including the requirement of at least one aroyl group, and the preference for two aroyl moieties.

Results and Discussion

II-2. Electrolysis of E,E-1,7-dibenzoyl-1,6-heptadiene (1a)

The cyclobutanations of substrates **1a** and **1g** (Scheme II-1) have previously been reported from these laboratories. Using lithium perchlorate (0.1 M) as the electrolyte, the reaction of **1a** was found to afford a total yield of pericyclic products (**2,3**) of just 45%, and the ratio of *trans*-**2**: *cis*-**2**: **3** was found to be 2.4:2.0:1. The total yield of pericyclic products obtained from **1g** was even smaller (35%).[5] Consequently, various electrolytes (and other procedural changes) were investigated in the present work in order to determine whether synthetically useful procedures might be developed for carrying out these novel reactions.



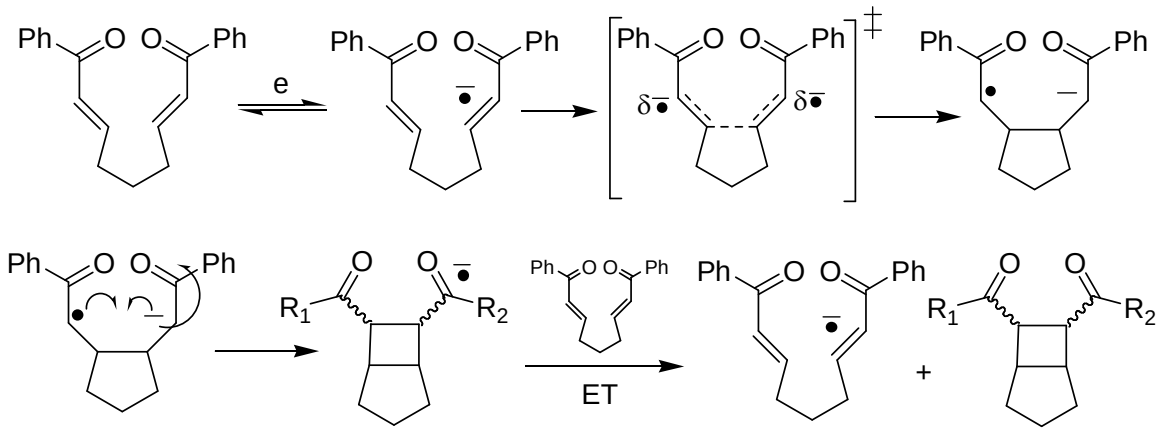
1 *trans*-**2** *cis*-**2** **3**

	X	$R_1 = R_2$		X	R_1	R_2
1a	CH_2	Ph	**1f**	CH_2	4-Ph-Ph	4-Ph-Ph
1b	O	Ph	**1g**	CH_2	Ph	CH_3
1c	CH_2	4-Cl-Ph	**1h**	CH_2	CH_3	CH_3
1d	CH_2	3,4-Cl_2-Ph	**1i**	CH_2	Ph	OEt
1e	CH_2	β-Naphthoyl	**1j**	CH_2	OEt	OEt

Scheme II-1. Pericyclic products in the electrocatalytic, intramolecular anion radical cyclobutanation reactions of various bis(enones).

The anion radical mechanism

The anion radical chain cycloaddition mechanism proposed for these reactions is rather novel and is summarized in Scheme II-2. According to this mechanism, reduction of the substrate at the cathode leads to a substrate anion radical, which then cyclizes to a distonic anion radical intermediate. This intermediate cyclizes to the anion radical of the cyclobutane product. The anion radical moiety presumably resides upon one of the benzoyl groups. Finally, exergonic electron transfer (ET) from the product anion radical to a molecule of the neutral substrate occurs, setting up the chain process and affording the neutral cyclobutane product. The distonic anion radical intermediate can also cyclize to a Diels-Alder adduct anion radical, where the anion radical moiety again resides upon a benzoyl moiety.



Scheme II-2. Proposed mechanism for the anion radical chain cyclobutanation reaction of, for example, 1,7-dibenzoyl-1,6-heptadiene (**1a**).

Tetraalkylammonium tetrafluoroborate electrolytes

The use of tetraalkylammonium tetrafluoroborates as electrolytes was explored on the assumption that ion pairing to the tetraalkylammonium cation should be much looser than with the lithium ion, resulting in a possible increase in reactivity of the anion radical intermediates. In fact, in the case of **1a,** a dramatic increase in yield to 88% was observed under these conditions. As will be noted in Table II-1, the yield of the *trans* cyclobutane product (*trans*-**2**) is elevated to 59%. Since the *cis* isomer (obtained in 17% yield) is readily isomerized to the *trans* isomer under acidic or basic conditions, this reaction sequence makes the *trans* isomer available in an overall 71% yield. The novel Diels-Alder product (**3**), obtained in 13% yield, is also of inherent interest in that it represents the first documented instance of an anion radical Diels-Alder reaction. Since complete conversion of **1a** to products is accomplished after a maximum[9] of 21% of the theoretical

charge had flowed, the reaction is mildly electrocatalytic, with a catalytic factor of 4.7 (representing a 0.21 F mol^{-1} process).

Table II-1. Yields and catalytic factors for the electrocatalytic intramolecular anion radical pericyclic reactions of various bis(enone) substrates (**1**).

Substrate	Proce-dure[a]	Yield of *trans*-**2**	Yield of *cis*-**2**	Yield of **3**	Total Pericyclic yield	Other Products	Catalytic Factor
1a	A	59%	17%	13%	88%	-	4.7
1b	A	39	11	3	53	**4b**; 11%	11
1b	B	21	20	2.0	43	-	1.6
1b	C	21	39	28	88	-	1.8
1c	A	52	11	12	75	**5c**; 5%	5.1
1d	B+C	7	33	16	56	**6d**; 6%	1.3
1d	D	3	0	0	3	**5d**; 17%[b]	7.3
1e	A	29	14	8	51	**5e**; 17%	5.2
1f	C	7	21	25	53	**6f**; 13%, **7f**; 7%	1.9
1f	A	12	0	0	12	**5f**; 17%	1.4
1g	C	0	9	0	9	**7g**; 30%[c]	<1
1g	D	19[d]	0	0	19	-	1.8
1i	B	32[e]	0	0	32	-	<1
1j	D	0	0	0	0	**5j**; 42%	4.5

[a] The electrolytes used in the respective procedures were: A=0.1M tetrabutylammonium tetrafluoroborate; B=0.1M lithium perchlorate; C=0.1M magnesium perchlorate; D=0.1M tetraethylammonium tetrafluoroborate.

[b] Also obtained 35% of an unidentified polymer

[c] Two isomers

[d] Both *trans* isomers were observed: 12% and 7% (~2:1 ratio), x-ray of major isomer provided.

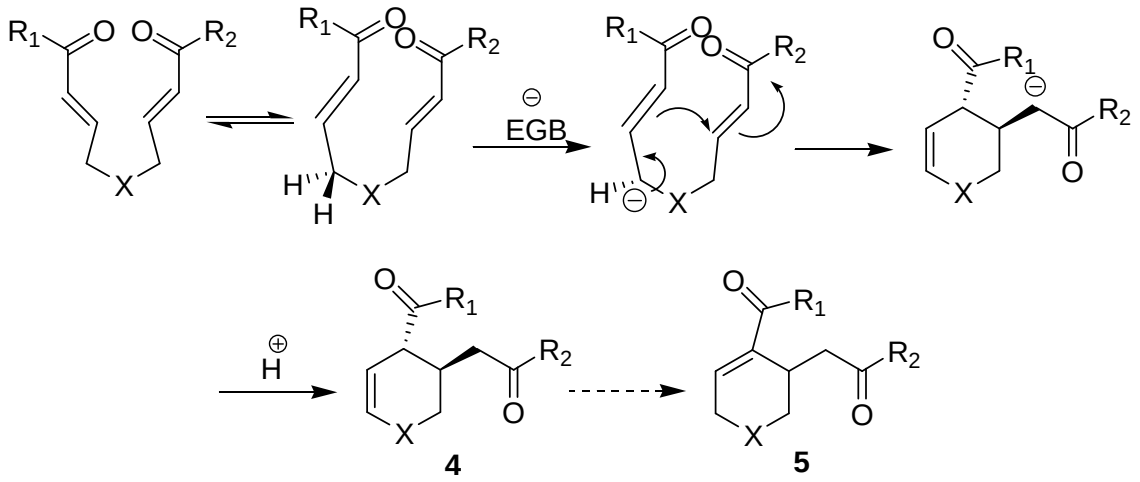
[e] Both *trans* isomers were observed: 28% and 4% (7:1 ratio).

II-3. Electrolysis of E,E-1,7-dibenzoyl-4-oxa-1,6-heptadiene (1b)

Effect of electrogenerated bases

The extension of this chemistry to the ethereal substrate **1b** was investigated next. Under conditions similar to the earlier work (using lithium perchlorate as the electrolyte)[5] a total yield of 43% of pericyclic products was isolated, with *trans*-**2b** being the major product. Under both the present and earlier work's conditions the catalytic factor was <3. When tetrabutylammonium tetrafluoroborate was used as the electrolyte, pericyclics were isolated in 53% yield. Interestingly, this reaction proceeded somewhat more efficiently in terms of the catalytic factor (11) than any of the other reactions, but the yield of pericyclic products was diminished in comparison to the corresponding electroreduction of substrate **1a** when using the same electrolyte because of a competing reaction of the substrate (Scheme II-3). The formation of **4b** implies a base catalyzed deprotonation of **1b**, followed by a Michael type addition of the conjugate base *via* the alpha carbon of the extended enolate to the beta carbon of the enone moiety. Formation of this product in the reaction using tetrabutylammonium tetrafluoroborate as the electrolyte, and not with any of the other electrolytes, is in agreement with the postulate that the intermediate anionic species are less tightly ion paired under these conditions, and are therefore substantially more reactive (basic). Since a product analogous to **4b** was not observed in the electrochemical reaction of **1a**, it is apparent that the substitution of oxygen for carbon tends to acidify the adjacent C-H bond. A similar competition has been reported in the electrohydrocyclization of butenolides.[10] In the case of substrate **1b**, a product corresponding to the isomerization of the double bond, into conjugation with the carbonyl group, was not observed. However, in several other instances products corresponding to

such a structure, **5**,[11] were obtained instead of **4**. The nature of the electrogenerated base (EGB)[12,13] species responsible for the deprotonation is unknown, but likely candidates might be a substrate or product anion radical or a dianionic intermediate produced by further reduction of the proposed distonic anion radical intermediate.



Scheme II-3. The electrogenerated base (EGB) catalyzed products (**4** and **5**) obtained in the electrochemical reduction of substrates **1,** in the presence of tetraalkylammonium tetrafluoroborate as the electrolyte. When X = O product **4** is formed, when X = CH_2 product **5** is formed.

Use of $Mg(ClO_4)_2$ electrolyte

Although the use of tetraalkylammonium tetrafluoroborates as the electrolyte appears to be the more general method of choice for carrying out most of these anion radical cycloadditions with optimal efficiency, in the specific case of **1b** the competing reaction described above tended to lower the yields of the pericyclic products. In view of that, it appeared worthwhile to investigate the effect of using a more strongly ion-pairing

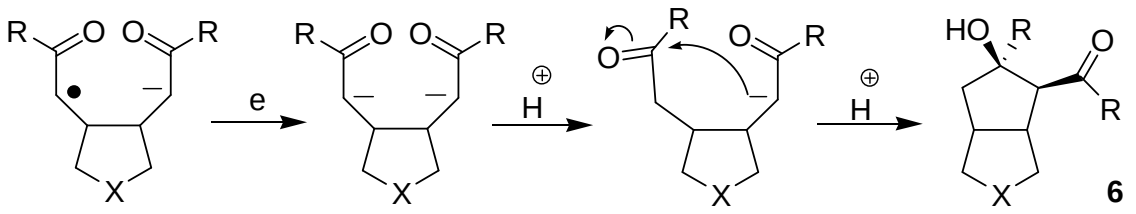
counterion than even the lithium ion, i.e., the magnesium ion. When the electrochemical reaction was carried out in the presence of magnesium perchlorate as the electrolyte, an 88% yield of pericyclic products was obtained. The increase in the *cis/trans* ratio in the cyclobutane product may also reflect the stronger ion pairing between the magnesium ion and the anion radical moiety in the transition state for the final cyclization step.

II-4. Electrolysis of E,E-1,7-bis(4-chlorobenzoyl)-1,6-heptadiene (1c)

It had been found in the previously reported work[5] that the introduction of electron donating substituents, such as 4-methoxy, onto the aryl ring of **1a** sharply inhibits cyclobutanation. It is presumed that this is the result, at least in part, of the inability of the distonic anion radical intermediate to cyclize to the product cyclobutane anion radical, which would require the anion radical moiety to reside in a higher energy SOMO (that of a 4-methoxybenzoyl moiety) than in the case of the unsubstituted substrate. Consequently, the facility of bis(enone) anion radical cyclobutanation of substrates that would provide a lower energy product anion radical SOMO was investigated. Substrate **1c**, which has electron withdrawing 4-chloro substituents on both of its benzoyl groups, was found to undergo smooth anion radical cycloaddition under the tetrabutylammonium tetrafluoroborate electrolyte conditions, affording a 75% yield of total pericyclics, of which 52% was the *trans* cyclobutane. It is of special interest that the chlorine substituent is retained in the product, even though the 4-chlorobenzoyl anion radical moiety was potentially susceptible to chloride ion loss. Presumably, electron transfer from the product anion radical to substrate is sufficiently rapid as to suppress the potential loss of chloride ion.

II-5. Electrolysis of E,E-1,7-bis(3,4-dichlorobenzoyl)-1,6-heptadiene (1d)

The introduction of an even more strongly electron withdrawing *meta* chloro substituent into the substrate, in addition to the *para* chloro substituent, as in substrate **1d** would be expected to accelerate the rate of the second cyclization step even further by providing a lower energy SOMO for the product anion radical. However, the considerably increased stabilization of the substrate anion radical, and the expected shift in electron density in the SOMO from the alkene moiety to the now rather strongly electron-deficient aroyl ring could also be expected to have an adverse effect upon the rate of the first cyclization step. In accord with the latter idea, when **1d** is electrolytically reduced in the presence of the tetraethylammonium tetrafluoroborate electrolyte, the yield of pericyclic products falls precipitously to 3%, the main products consisting of a 17% yield of a base-catalyzed cyclization/isomerization product (**5d)** and an uncharacterized polymer (35%). However, in the presence of a mixed lithium perchlorate/magnesium perchlorate electrolyte, the desired pericyclic reactions are observed to occur with moderate efficiency, but the yields of the pericyclic products are lower than in the case of **1c**, and an aldol-type product (**6d**) is also formed. This latter product is considered to result from reduction of the intermediate distonic anion radical to a dianion, which subsequently is protonated and undergoes cyclization (Scheme 4).



Scheme II-4. Formation of an aldol-type side product (**6**), *via* reduction of the distonic anion radical to an enolate dianion.

II-6. Electrolysis of E,E-1,7-di-1-naphthoyl-1,6-heptadiene (1e) and Electrolysis of E,E-1,7-bis(4-phenylbenzoyl)-1,6-heptadiene (1f)

The replacement of the phenyl group with a β-naphthyl or 4-biphenylyl group could also provide a more suitable venue for the stabilization of the anion radical of the product than in the case of **1a**, but again the lowering of the SOMO energy and the shifting of the SOMO density toward the aroyl moiety could retard the first cyclization step. The cyclobutanation of substrate **1e** (which has β-naphthyl substituents), using tetrabutylammonium tetrafluoroborate as the electrolyte, was found to proceed, albeit in moderate yield (51%), suggesting that the predominant effect of the increased delocalization provided by the naphthyl group is the lowering of the SOMO energy and the shift in density away from the alkene linkage. However, the retardation of the cyclization is evidently much less than in the case of the dichloro substrate **1d**. As in this latter case, the base-catalyzed cyclization/isomerization product **5e** was also formed (17%; Table II-2). It is worth noting that when the reaction is not run to completion (~80% complete), the yield of pericyclic products is relatively unchanged, but the amount of the base catalyzed product is greatly reduced. This may well be indicative of a build up of electrogenerated bases within the solution, accelerating the cyclization to **5** in the latter

stages of the reaction. This build up of base could also provide an explanation for the increase in the *trans:cis* ratio observed in the more complete reaction.

Table II-2. The effect of the extent of reaction upon the yields of anion radical and base-catalyzed products.

Substrate[a]	Yield of *trans*-**2**	Yield of *cis*-**2**	Yield of **3**	Total Pericyclic yield	Other Products	Catalytic Factor
1e	29	14	8	51	**5e**;17%	5.2
1e[b]	17	21	10	48	**5e**; 6%	5.4

[a] The electrolyte was 0.1M tetrabutylammonium tetrafluoroborate.

[b] Reaction run to 79% completion (based upon recovered **1e**), yields and catalytic factor are corrected for **1e** recovery.

Substrate **1f**, which contains 4-biphenylyl moieties, responds in a manner rather similar to that of **1d**. Limited *trans*-**2f** formation is observed, along with greater formation of the base-catalyzed cyclization/isomerization product **5f** (tetraalkylammonium electrolyte). However the use of $Mg(ClO_4)_2$ afforded a moderate pericyclic yield of 53%. Substrate **1f** has limited solubility in acetonitrile, so that these reductions were carried out in 1:1 THF:acetonitrile solutions.

II-7. SOMO requirements for cyclization

Electrolysis of **E,E-1-acetyl-7-benzoyl-1,6-heptadiene (1g)** and **E,E-1,7-diacetyl-1,6-heptadiene (1h)**

In contrast to the aroyl groups considered above, acetyl groups provide a much less extensively delocalized, higher energy SOMO for the product cyclobutane or Diels-Alder anion radical. The potential anion radical pericyclic chemistry of substrate **1h,** which has two acetyl substitutents, was therefore not expected to be as efficient as when aroyl groups are present. In accord with this supposition, no pericyclic products at all could be detected in the electroreduction of this substrate.

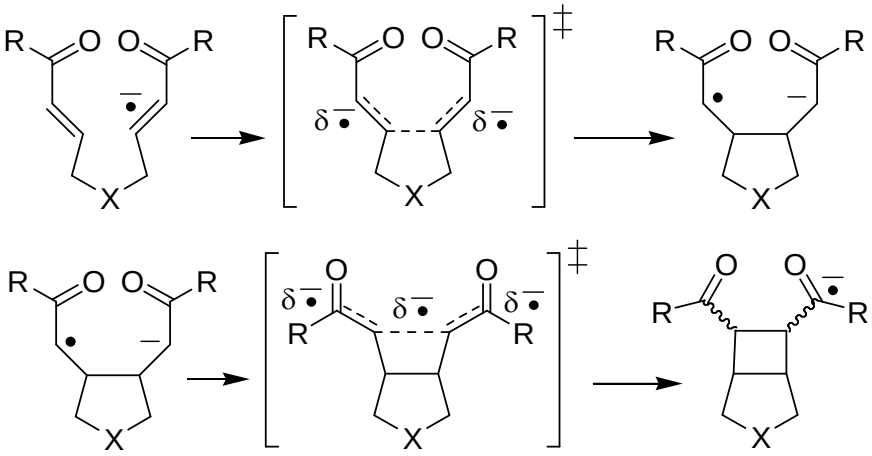
However, since the anion radical of the pericyclic products only requires (and perhaps can only utilize) a single aroyl moiety, it was considered likely that pericyclic chemistry might occur with unsymmetrical substrate **1g**, which has one benzoyl and one acetyl substituent. The previously reported results, using lithium perchlorate as an electrolyte, have already confirmed this conjecture, but further experiments were carried out in the present work in connection with magnesium perchlorate and tetraethylammonium tetrafluoroborate as the electrolytes. The observed yields in both cases are quite modest. However, an additional feature of interest emerges when tetraethylammonium tetrafluoroborate is used as the electrolyte, namely, that both possible *trans*-**2g** isomers are formed, in a 2:1 ratio, with the major cyclobutane having the benzoyl group *syn* to the cyclopentane ring.

Electrolysis of **E,E-7-ethoxy-1-benzoyl-1,6-heptadiene (1i)**

The reduction of **1i**, which has one benzoyl and one carboethoxy substituent, provides a still further example of the relative inefficiency of pericyclic chemistry when only a single benzoyl group is present. When electrolyzed in the presence of lithium perchlorate, **1i** provides a 32% yield of two isomers of *trans*-**2i.** The major isomer appears, on the basis of NMR comparisons, to be structurally analogous to the major *trans*-**2g** isomer obtained from **1g**. This reduction is unusual in that it is not catalytic. An intriguing possible interpretation of this data is that while benzoyl reduction is occurring readily and reversibly, the initial cyclization step is sharply retarded by the ineffectiveness of the ester function at delocalizing and stabilizing the SOMO in the transition state. This could require cyclization to occur *via* the rarer reduction of the unsaturated ester function. This higher energy anion radical could then rapidly cyclize to the reactive benzoyl ene function. The key factor here is that catalysis would necessarily involve electron transfer from a product anion radical to a substrate molecule, and this chemical electron transfer undoubtedly is highly selective for formation of the more stable, and apparently unreactive, anion radical corresponding to the benzoyl enone function. Additionally, this chemical electron transfer is likely to be irreversible in nature, halting catalysis. The chemically reduced substrate may prove reactive in non-cyclobutanation mechanisms, which may account for the observed low yield.

Diminished cyclization rates

Since the desired pericylic reaction products provide the required low energy SOMO associated with an aroyl function (in this case, benzoyl), and the starting substrate provides a readily reducible aroyl enone function, it appears likely that the lower efficiency of the desired pericyclic chemistry in the substrates which contain only a single aroyl function must arise from diminished cyclization rates in either one or both of the cyclization steps. It therefore seems reasonable to propose that, in the transition states for both cyclization steps, the SOMO is at least partially delocalized over both enone moieties, as indicated in Scheme II-5. The delocalization is presumably greatest, and the SOMO energy the lowest, when both keto functions are of the aroyl type.



Scheme II-5. Proposed delocalization of the SOMO over both carbonyl groups in the transition states for both cyclization steps.

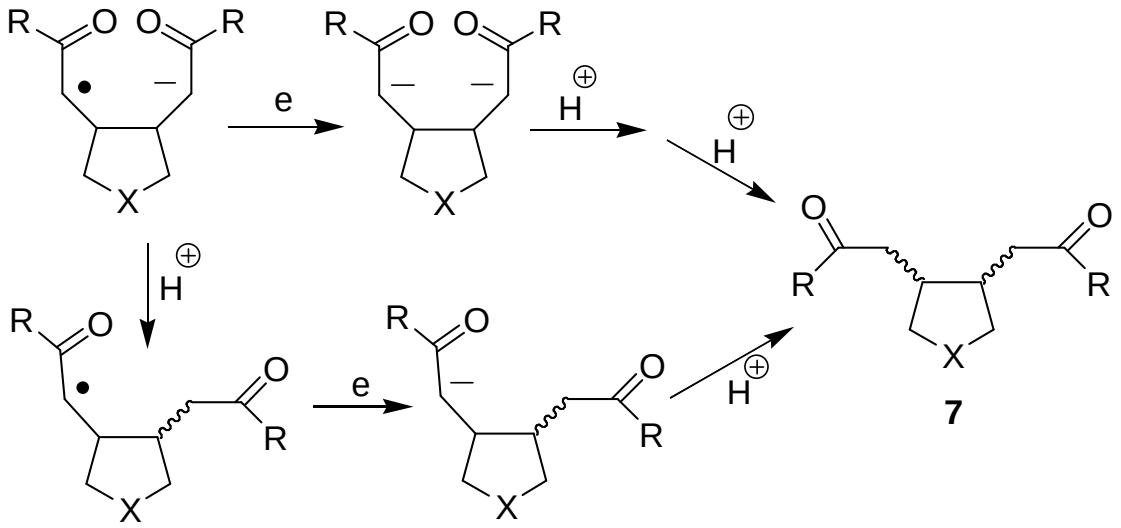
II-8. Evidence for the distonic anion radical intermediate

In most cases the electrolyte systems (lithium/magnesium perchlorate or tetraalkylammonium tetrafluoroborate) lead to the formation of a mixture of the *cis* and *trans* cyclobutane isomers. At the earliest point of the electrochemical reactions at which these products could be detected, the *trans* cyclobutane was always formed in modest excess over the *cis* isomer. As the reaction progressed further toward completion, the *trans:cis* ratio progressively increased. The values given in Table 1 correspond to reactions run essentially to completion. This progressive change in the *trans:cis* ratio suggested the possibility that a portion of the *cis* isomer was being isomerized to the more stable *trans* isomer in the course of the reaction. Although a base-catalyzed isomerization was formally a possibility, it also appeared possible that anion radicals of the *cis*-cyclobutane were being re-formed during the reaction and subsequently reverting to the distonic anion radical, which could once again cyclize to give either cyclobutane isomer or the Diels-Alder adduct. A distinction between these two mechanistic possibilities is therefore possible, based upon the predicted formation of small amounts of the Diels-Alder adduct in the latter mechanism. To test this possibility, isomers of **2b** were isolated and used in electrolysis reactions with lithium perchlorate as the electrolyte. A quantity of *cis*-**2b** was reduced in isolation, leading to the formation of *trans*-**2b** (32%), **3b** (7%), an aldol product **6b** (11%), a dihydrocyclopentane product **7b** (20%; see Scheme 6), with a further 18% of unreacted *cis*-**2b.** The attempted reduction of *trans*-**2b**, as expected, failed to lead to any reaction. A degree of reactivity was seen under extreme conditions (very negative potentials, large amounts of charge). Although some *trans*-**2b**

was still returned, no other known products were obtained. This clearly indicates that, while the *trans* isomer is stable toward continued reduction at normal potentials, the *cis* isomer readily reverts to the proposed distonic intermediate. This not only allows for the formation of the *trans* and Diels-Alder products, but also of **7b**, which represents protonation after the first cyclization, effectively "trapping" the distonic anion. In further accord with the postulate of *cis*-*trans* isomerization *via* regeneration of the distonic anion radical intermediate is the previously discussed absence of any base-catalyzed products (e.g., **4** and **5)** in any perchlorate reaction system. Since the distonic anion radical intermediate is evidently involved in the reversal of the cycloaddition, an application of the law of microscopic reversibility strongly suggests that the forward reaction also involves the same distonic intermediate.

Table II-3: Effect of a weak acid in solution during electrolysis (of **1e**), trapping the distonic anion and reduction of electrogenerated base products (in this case, **5e**).

Additive	%Yield of *trans*-**2e**	%Yield of *cis*-**2e**	%Yield of **3e**	%Yield of **5e**	%Yield of **6e**	%Yield of **7e**	%Yield of products
None	29	14	8	17	0	0	68
1.6 Molar excess of acetic acid	6	0	0	3	14	38	61



Scheme II-6: Mechanism of formation of the "dihydro" product, **7**, via protonation of the distonic intermediate. Two plausible routes shown, reduction to dianion followed by two protonations, and protonation-reduction-second protonation.

Trapping of the distonic anion radical intermediate/Inhibition of EGB pathway

It was thought that addition of a slight excess of a weak acid would not only inhibit EGB pathways but would also trap (protonate) the proposed distonic anion radical. Indeed this was realized with a 1.6 molar excess of acetic acid placed in the solution from the beginning of electrolysis. The naphthoyl substrate **1e** was chosen as it leads to modest base-catalyzed product formation (17% of **5e**). The expected trapping is clearly the dominant mechanism, represented by both **6e** and **7e** formation (Table II-3). The expected reduction in base-catalysis (product **5e**) is also seen, down to just 3%. Also, by limiting the excess of acetic acid, we were still able to obtain small amounts of our primary cyclobutanation product (*trans*-**2e**), although formation of *cis*-**2e** and **3e** were reduced to levels below detection. The proposed mechanism for the formation of **7** is given in Scheme II-6.

II-9. Mediated Electrolysis

The possibility of developing a mediated electrochemical reduction method was also probed. The strategy adopted was to provide a mediator which is (in the ideal case, selectively) reduced at a less negative potential than the substrate, and which forms a relatively long-lived anion radical capable of mildly endergonic electron transfer to the substrate molecules.[14-16] This strategy should provide for a low substrate anion radical concentration, which could minimize anion radical to anion radical coupling as well as over-reduction of the substrate (dianion formation). Initial attempts utilized **1b** as the substrate and magnesium or lithium perchlorate as the electrolyte. Benzil (diphenyl diketone), dypnone (E-3-phenyl-2-butenoylbenzene), and benzophenone were investigated as mediators, but all three proved to be ineffective. Mediator reduction did occur at less negative potentials (as evidenced by a temporary solution color change) than that of the substrate, but products did not form until the potential was reduced to the usual value for reduction of the substrate.

Further studies were directed toward the use of tetraethylammonium tetrafluoroborate as the electrolyte, this time using **1c** as the substrate. Although these conditions failed to provide an increase in yield of pericyclic products, they did provide important insights into the interplay between anion radical cyclization and electrogenerated base catalysis (Table II-4). Benzophenone reduction was found to occur at nearly the same potential as for **1c**, when benzil reduction occurred at a much less negative potential. In the case of benzil, this occurred at a potential that did not lead to substrate reduction, so no pericyclic products were formed. On the other hand, in the absence of a mediator, base-catalyzed products (such as **5c)** were formed in a low yield.

When benzophenone was employed as the mediator, both types of products were formed, indicating that both the substrate and mediator are being reduced at the cathode.

Table II-4. Anion radical vs base-catalyzed reactions in the mediated electrolysis of **1c**, where mediation is ineffective at increasing anion radical product formation (products **2-3**), yet boosts electrogenerated base products (**5**).

Mediator	% Yield of *trans*-**2c**	% Yield of *cis*-**2c**	%Yield of **3c**	% Yield of **5c**
None	52	11	12	5
Benzophenone	42	11	7	13
Benzil	0	0	0	28[a]

[a] Along with 42% unidentified polymer.

Apparently, anion radical cyclobutanation occurs only when the substrate is reduced, and reduction of the mediator leads essentially only to the base-catalyzed reaction. These observations indicate that the desired mildly endergonic electron transfer is too slow to compete wth the base -catalyzed reaction

Efficient base-catalyzed reactions

The observations noted above immediately suggested the possibility of employing an excess of benzil to engender a highly electrocatalytic method for selectively and efficiently forming the base-catalyzed product. This possibility was realized in the case of the electrochemical reduction of **1b** in the presence of a relatively large excess of benzil, which gave only **4b**, in 68% yield. The catalytic factor here was rather modest at 2.8, although low concentrations of starting material and a large excess of benzil made judging the end of the reaction difficult. Comparison of this result with that obtained for **1c** (with benzil) suggests that the use of mediators to engender these base-catalyzed cyclizations may prove problematic, due to competition with polymerization. The efficiency seen with formation of **4b** may be engendered by the greater acidity of the protons (alpha to the bridging oxygen) in **1b**.

Other bis(enone) substrates

A brief selection of further bis(enones) were studied, all were run in electrolyses with perchlorate and alkylammonium electrolytes. A mixed -Naphthoyl/phenyl bis(enone), which appeared to give trace amounts of several different cyclobutanes, but further synthesis of substrate was not considered time effective. Rather surprisingly, a bis-phenylsulfonyl-enone did not undergo cyclobutanation, or indeed any cyclization. This contrasts to the rather facile intermolecular cyclobutanation of phenyl vinyl sulfone.[3] There are two possible explanations for this failure, firstly a steric effect due to the bulk of the sulfonyl group, such that this bis(enone) prefers an elongated conformation. Sulfonyl goups are seen to be effectively rather bulky, as observed in chapter five with the structure of product **10**. Secondly, perhaps the anion radical that is formed by

reduction of one enone moiety is too short lived, that is to say too reversible, and therefore not present for long enough for the appropriate conformation to occur and allow for the initial cyclization step.

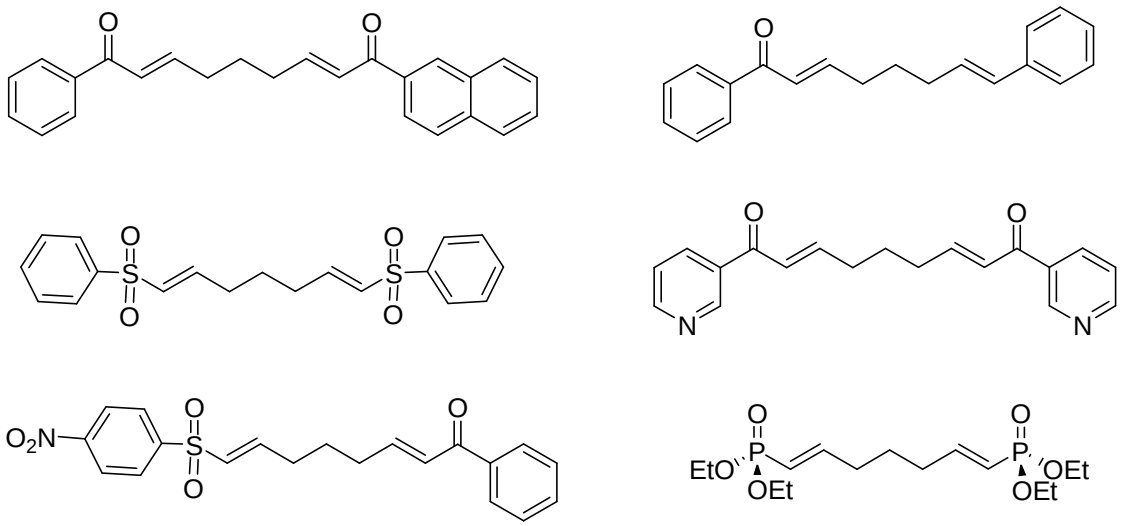


Figure II-1. Selection of additional bis(enones) studied, electrolyses were carried out with alkylammonium and perchlorate electrolytes.

The other four substrates shown similarly showed no sign of recognizable cyclization, although they were generally consumed through the course of the electrolysis, presumable via polymerization, or decomposition. The nitro-phenyl sulfonyl compound is thought to be too reducible, as evidenced by the rather low applied potential (<-1.0 V) required to give solution coloration.

Conclusions

This chapter details the development of conditions for carrying out electrochemically initiated, intramolecular anion radical cyclobutanations of bis(enones) and related substrates in high yields and with substantially less than the theoretical consumption of electricity (i.e., electrocatalytically). The solvent/electrolyte combination acetonitrile/tetraalkylammonium tetrafluoroborate is found to be an especially effective one for producing high yields and large catalytic factors. The formation of novel anion radical Diels-Alder adducts in minor amounts is also verified. The scope and limitations of these reactions are rather extensively explored and defined. In particular, the reactions have been found to have an absolute requirement for at least one aroyl ketone moiety and a significant preference for both ketonic moieties to be of the aroyl type. Theoretical rationales for these requirements and preferences are presented. Strongly electron withdrawing substituents (upon the aroyl moiety) tend to decrease reaction efficiency by diminishing the rate of the first cyclization step, such that a competition between anion radical mediated and electrogenerated base-catalyzed reactions is observed. Evidence for a stepwise (as opposed to concerted) cycloaddition mechanism involving a distonic anion radical intermediate is presented, and the distonic anion intermediate has been trapped.

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CHAPTER III

Electrolyte directed diastereoselectivity of bis(enone) cyclization

III-1. Introduction

Intramolecular anion radical pericyclic reactions of tethered bis(enones) have been described from these laboratories.[1] These anion radical reactions are of special interest because they represent rare examples of intramolecular anion radical cycloaddition, rather than the more common electrohydrocyclization (EHC). The focus of this work has been in the comparison of electrochemical methods to chemical reduction routes,[2] and the elucidation of the full mechanism of cyclization.[3] While undertaking this investigation we became aware that the electrolyte choice was having a strong effect upon the ratio of products obtained from each reduction. To further explore this feature, the effect of several perchlorate electrolytes was studied. The commonly used $LiClO_4$,[1,3-7] $Mg(ClO_4)_2$,[1-5,7-10] $NaClO_4$,[6,7,10-12] $KClO_4$,[12] and $AgClO_4$[13] were investigated, as well as what may represent the first use of $Ba(ClO_4)_2$[6-8] in an electrosynthetic application.

The product ratios were studied in a rather novel way. The reactions were run on a small scale (~60mg), and the crude product analyzed by ^1H NMR to determine the ratio of products formed. This was possible due to the exclusion of perchlorate during workup, that all products had at least one non-overlapping absorption, and all products had previously been fully characterized. Additionally, this approach allows for greater accuracy in the determination of ratios, by reducing rounding errors (after separation) and the chance of disproportionate losses in separation. The percent reaction completion,

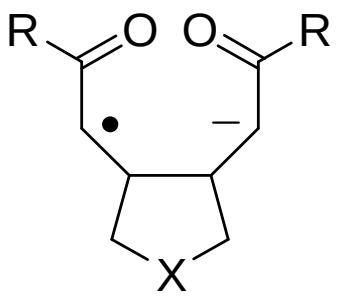
stated in tables below, is extrapolated from an estimate of unreacted starting material (again from the crude NMR), which is then used to arrive at the maximum percent of charge used. A maximum percent charge of, say 50%, would indicate that the number of electrons that flowed through the solution was equal to half the number of moles of substrate bis(enone) that reacted, or a catalytic factor of two. However, as will be discussed, some of this charge is clearly consumed by other processes (particularly in experiments that are run for longer), such that the actual amount of charge consumed by the substrate is lower than the maximum stated. The experimental section gives more detail, using fully separated sample reactions to validate this approach.

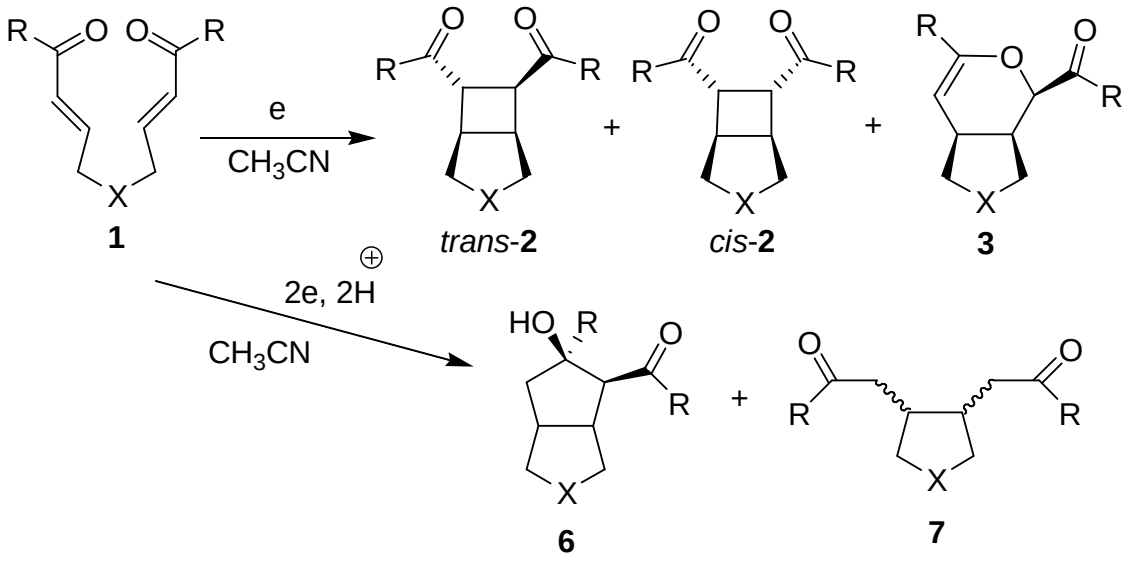
This work represents the first observation of such an electrolyte effect in cyclobutanation. A similar effect has been observed in a handful of EHC systems, with a relatively limited array of electrolytes.[4,5] The use of a strong acid or base (as the electrolyte) has been seen to affect the isomer ratios of products in ketone to alcohol reductions,[14,15] and in diketone to diol EHC.[16] Indeed solvent choice has also been observed to affect the ratios of product isomers in EHC[16] and reductive cleavage,[17] as well as in non-electrochemical deprotonations.[18] However, such solvent effects tend to be of a more modest magnitude than those observed in the present work. There are also numerous cases of electrolyte choice affecting the ability of a reaction to proceed.[19]

The bis(enones) studied have been observed to readily undergo cycloaddition under electrochemical reduction conditions.[1] This cycloaddition is considered to occur via a two-step mechanism,[3] involving a distonic anion radical intermediate, shown below (Fig. III-1). Virtually all products issue from this distonic species, and the three primary

pericyclic (two cyclobutanation and one Diels-Alder) products result from its subsequent cyclization/cyclobutanation. The proportion of products **6** and **7**, which represent two-proton EHC processes, is determined by the lifetime of the distonic intermediate (in turn controlled in part by the relative SOMO stabilizing power of the R group). Use of an alkylammonium electrolyte is favored for these pericyclic conversions, partly for its higher electrocatalysis (generally representing 0.2 F mol^{-1} processes) and partly for the greater pericyclic yields obtained.[3] However, perchlorate electrolytes also display modest electrocatalysis (0.6 to 0.8 F mol^{-1}), along with reasonable pericyclic yields, which are somewhat diminished by the competing formation of products **6** and **7**.

Figure III-1. The distonic anion intermediate formed from the initial cyclization; products **2** through **7** are all formed in competing reactions from this intermediate species.





Substrate	R	X
1b	Ph	O
1c	4-Cl-Ph	CH_2
1d	3,4-Cl_2-Ph	CH_2
1e	β-Naphthoyl	CH_2
1f	4-Ph-Ph	CH_2

Figure III-2. The bis(enone) substrates studied, the primary pericyclic products (**1** – **3**), and two proton electrohydrocyclization (EHC) products (**6** – **7**).

III-2. Electrolyte variation in the reduction of E,E-1,7-bis(4-chlorobenzoyl)-1,6-heptadiene (1c)

The 4-chlorophenyl bis(enone) substrate **1c** was chosen for the preponderance of the electrolyte variation experiment, primarily because of its greater tendency to form the three pericyclic products exclusively. Additionally, **1c** is also conveniently solid at room temperature. Lithium and magnesium perchlorate were studied initially. They reveal a large variation in the isomer product ratio upon switching from the +1 to the +2 cation. The Mg^{2+} greatly retards the formation of the thermodynamically favored *trans*-**2c**

cyclobutane isomer (discussed below). This clearly suggests a much stronger chelation of the Mg^{2+} ion with the distonic anion and, in particular, in the transition state leading from this latter to the product anion radical. Effectively, the divalent metal ion steers the two oxygen functions of the intermediate distonic anion radical into the relatively close positioning involved in *cis*-**2c** and **3c**, where the chelating interaction can be maintained in the product anion radical, and away from the distant positioning required in *trans*-**2c**, where the metal cation would be able to interact with only one of the two oxygen functions. The formation of a small amount of **6** indicates that even the aldol cyclization route can compete in what is essentially an aprotic system.

Table III-1. Product isomer variation with electrolyte using substrate E,E-1,7-bis(4 chlorobenzoyl)-1,6-heptadiene (**1c**) in acetonitrile.

	Electrolyte	Ratio of *trans*-**2c**	Ratio of *cis*-**2c**	Ratio of **3c**	Ratio of **6c**	Percent reaction completion	Maximum percent of charge used
1	0.1M $LiClO_4$	1	1.4	0.45	-	77	86
2	0.5M $LiClO_4$[a]	1	1.0	1.5	0.12	91	15
3	0.1M $LiClO_4$ + 0.006M $AgClO_4$	1	2.3	0.57	1.9	59	95[b]
4	0.1M $NaClO_4$	1	0.77	0.32	-	86	16
5	<0.05M $KClO_4$	1	0.12	0.21	-[c]	100	14
6	0.1M $Mg(ClO_4)_2$	1	6.4	2.9	0.58	81	27
7	0.1M $Ba(ClO_4)_2$	-	1	0.94	0.72	79	53

[a]Using THF as the solvent.

[b]Competing silver ion reduction, 25 C were used, substrate and silver ion used correspond to 9.1 C and 17.2 C, respectively.

[c]0.51 ratio of an electrogenerated base product.[3]

The use of barium perchlorate as the electrolyte takes this effect to a rather stunning and unprecedented extreme, where all *trans*-**2c** formation is suppressed. In fact, *cis*-**2a** and **3** are formed in nearly equal amounts, and in a slight excess over **6**. This result is especially intriguing in that, because of the much smaller charge-to-size ratio of the barium ion than the magnesium ion (the ionic size of Ba^{2+} is 0.134 nm, whereas that of Mg^{2+} is only 0.064 nm), the former is expected to be inherently much less efficiently solvated than the latter. Evidently, the greater size of the barium ion provides a better fit to the chelation cavity available in the distonic anion radical than does the much smaller Mg^{2+}, thus enabling Ba^{2+} to efficiently interact with both oxygen functions (shown in Figure III-3). The data suggest that the Ba^{2+} cation also favors the Diels-Alder cyclization route, as this nearly 1:1 ratio to *cis*-**2c** is one of the highest seen in these experiments. It is appropriate to note that the two oxygen functions in **3** are in relatively close proximity, permitting a 5-membered chelation ring.

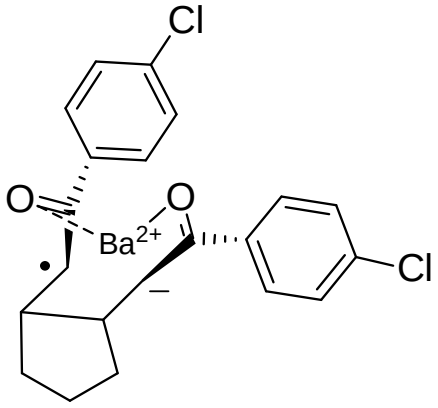


Figure III-3. Proposed chelation of Barium cation, with distonic anion intermediate, enforcing *cis* orientation of carbonyl moieties.

The normal effect of changing the charge to size ratio can be observed in the Li^+, Na^+, and K^+ series (expts. 1, 4, and 5, from Table III-2), where we see that, as the charge-to-size ratio decreases, chelation is rendered progressively less efficient, such that *trans*-**2c** formation can dominate. In fact, this *trans* preference approaches a factor of ten with potassium. The looseness of the ion pairing with the potassium ion even allows for an electrogenerated base-catalyzed product to form (usually only seen with the weakly ion-pairing alkylammonium salts).[3] It is known that the *trans*-**2** isomer is the thermodynamically more stable cyclobutane product. However, in most cases the *cis*-**2** isomer is formed in excess initially, indicating a kinetic advantage in the formation of this isomer, probably due to the strength of cationic chelation, which tends to maintain the *cis* relationship of the two carbonyl groups in the transition state for the cyclization reaction. Clearly, the weaker chelation provided by the Na^+ and K^+ ions no longer provides this advantage.

The use of silver perchlorate is complicated by the reduction of Ag^+ to Ag metal. Used in isolation, silver metal forms on the Working Electrode, and the solution is unable to sustain a potential negative enough for substrate reduction. However, a small amount of $AgClO_4$ could be used in conjunction with $LiClO_4$. In this experiment (expt. 3), an effect of added silver ion upon the products ratios is clearly evident, so that any analysis of the data must assume a superimposed silver ion effect. The experiment was also run for longer times than other experiments due to continued Ag^+ reduction, which consumed much of the charge that flowed. This increased length of reaction tends to favor the enhanced formation of **6** (see III-3 below), but cannot be the basis for the slight increase in the amount of *cis*-**2c**. This increase may be due to Ag^+ chelation.

Solvent effect

Solvent variation was not extensively examined in this study. However, an experiment utilizing the less polar solvent tetrahydrofuran (THF) did reveal an interesting effect, a greater tendency toward the formation of the Diels-Alder product (**3**). The basis for this novel periselectivity effect is uncertain, but could indicate that chelation effects are still more important in the less polar solvent, and that these effects may be especially strong in the transition state leading to **3**.

III-3. Product reduction effects

Through the course of the reaction, as the substrate is consumed, the electrocatalysis not surprisingly becomes less efficient. The product ratios observed can be altered at this advanced stage of an electrolysis. This is not thought to be a large effect, and has been shown to proceed via reversion of the *cis*-**2** isomer back to the distonic intermediate.

Table III-2. The effect of length of electrolysis upon isomer ratios, using 0.1M $LiClO_4$ as electrolyte.

Substrate	Ratio of *trans*-**2**	Ratio of *cis*-**2**	Ratio of **3**	Ratio of **4**	Ratio of **5**	Percent reaction completion	Maximum Percent of charge used
1c	1	1.4	0.45	-	-	77	86
1c	1	0.44	0.46	-	0.46	100	100
1d[a]	1	1.6	0.41	0.95	-	66	33
1d[a]	1	1.1	0.37	0.82	-	100	74
1b[b]	1	0.97	0.09	-	-	99	63
1b[b]	1	0.17	0.17	-	-	100	78

[a]0.2 M $LiClO_4$ was used.
[b]Ratios from PTLC separated yields.

Reduction of the *trans*-**2** isomer in isolation gives no reaction, yet similar reduction of isolated *cis*-**2** gives all products (**2-7**), after a relatively large amount of charge has passed.[3] It seems apparent that reduction of the substrate is greatly favored over reduction of the products; otherwise *cis*-**2** yields would be greatly lowered. Similarly, more extensive formation of product **7** would also be expected, as a result of further reduction or protonation of the distonic intermediate, if this reversion were occurring earlier in the course of the reaction. To examine this possibility, the continued reduction of substrate **1c** was examined, using exactly 100% of the required charge, ignoring electrocatalysis, and therefore representing extensive over-reduction (see Table III-2). This lowered the *cis*-**2c** isomer ratio, with increased formation of product **5**, a product not seen when the reaction is stopped sooner. This large drop in *cis*-**2c** isomer ratio is repeated when **1b** is over-reduced. Although in this case products **6** and **7** are not seen, the *cis*-**2b** isomer ratio is reduced five-fold, and the **3** isomer ratio is doubled. However, it should be remembered that the distonic anion formed from substrate **1b** will have a slightly different chelation profile, due to the bridging ethereal oxygen. Indeed this structural feature may also fractionally lower the reduction potentials of the products, so that reversion to the distonic anion may be more prevalent. A third example, involving substrate **1d**, with a somewhat more modest over-reduction, leads to a smaller effect. In this case, the *cis*-**2d** isomer ratio is merely lowered by a third, while other ratios remain effectively constant.

These results clearly highlight the limited effect of *cis*-**2** reduction upon the isomer ratios, at least until the advanced stages of an electrolysis. Such an electrolysis run

to near completion (say 90%), should see minimal interference to product isomer ratios from *cis*-**2** reversion. The base-catalyzed interconversion of the *cis*-**2** to *trans*-***2*** isomer is a formal possibility, yet the lack of formation of any electrogenerated base products in all but the weakest of chelated cation systems (namely K^+) seems to discount such an interfering effect.

III-4. Isomer ratio variation in other substrates

Several other substrates were also examined with regard to the major effect observed when the electrolyte is varied from $LiClO_4$ to $Mg(ClO_4)_2$. The different aroyl substituents yield slightly differing results, but the broad picture remains unchanged. The stronger Mg^{2+} chelation leads to a strong inhibition of *trans*-**2** formation, and subsequent increase of other product yields, in particular in those of *cis*-**2**. For the two experiments with substrate **1d**, it seems reasonable to assume that the stronger chelation of the Mg^{2+} ion leads to the majority of reduction occurring with this cation chelated. This leads to the most dramatic increase in the *cis*-**2** ratio observed for this substrate, a tripling of the *cis*-**2d** ratio (although a six-fold increase was observed for substrate **1c**).

A further interesting feature of these results, also noted above for Ba^{2+}, is the enhancement of the Diels-Alder cyclization route (product **3**) provided by the +2 cations. This effect, observed for all of the substrates, is especially interesting to consider in terms of the ratio of the Diels-Alder adduct to each of the individual cyclobutane isomers. Formation of **3** is generally seen to increase five-fold in comparison to *trans*-**2** for all of the substrates examined, but the change in the relative amount of **3** compared to *cis*-**2** is more variable and appears to be dependent upon the SOMO-stabilizing ability of the R group. The result is that only a small enhancement (ca. 50%) in the relative amount of **3**

is observed for substrates **1c** and **1d**, whereas this effect increases to a 2.5-fold enhancement for **1e**, and an eight-fold enhancement for **1b**.

Table III-3. The effect of using $LiClO_4$ or $Mg(ClO_4)_2$ as electrolyte upon the electrolysis of varied bis(enone) substrates.

Substrate	Electrolyte	Ratio of *trans*-**2**	Ratio of *cis*-**2**	Ratio of **3**	Ratio of **6**	Ratio of **7**	Percent reaction completion[2]	Maximum Percent of charge used[21]
1d	0.2M $LiClO_4$	1	1.1	0.37	0.82	-	100	74
1d	0.1M $LiClO_4$ + 0.1M $Mg(ClO_4)_2$	1	3.1	1.8	0.85	-	100	76
1e	0.1M $LiClO_4$	1	3.1	0.48	0.52	0.48	78	86
1e	0.1M $Mg(ClO_4)_2$	1	5.6	2.2	2.3	1.6	71	94
1f	0.1M $Mg(ClO_4)_2$	1	4.1	5.2	1.9	1.3	73	54
1b[a]	0.1M $LiClO_4$	1	0.97	0.09	-	-	99	63
1b[a]	0.1M $Mg(ClO_4)_2$	1	1.9	1.4	-	-	67	50

[a]Ratios from PTLC separated yields.

Conclusions

Variation of the nature of the cation of the supporting electrolyte leads to dramatic variations in the product ratios for a variety of bis(enone) intramolecular cycloadditions initiated by electrochemical reduction. It is proposed that the strength of the chelating interaction between the metal cation and the two oxygen functions of the distonic anion radical intermediate directly relates to these product ratios. This effect is prominently observed when +2 cations are used in place of +1 cations. The resulting increase in chelation strength leads to greatly retarded formation of the *trans*-cyclobutane product. The most dramatic results are observed in the use of $Ba(ClO_4)_2$, where all *trans*-**2c** formation is inhibited. This effect is interpreted in terms of a size effect, in which the much larger barium ion just fits into the chelation cavity of the intermediate distonic anion radical. Stronger cation chelation is also observed to correlate with enhancement in the formation of the Diels-Alder product **3**. It is noted that the two oxygen functions in **3** are proximate enough to maintain an efficient chelation interaction.

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CHAPTER IV

Intermolecular Anion Radical Cyclobutanation Reactions

IV-1. Introduction

Cyclobutanation reactions of the cation radicals of alkenes with neutral alkenes have by now become rather commonplace and are characterized by impressively high cycloaddition rates and low activation barriers, especially in comparison to the corresponding thermal reactions.[1] There have been some recent indications that this extensive body of cation radical cyclobutanation chemistry may have a close counterpart in the domain of anion radical chemistry. Specifically, the reduction of phenyl vinyl sulfone under electrochemical conditions (mercury pool cathode) has been reported to yield *trans*-1,2-bis(phenylsulfonyl)cyclobutane.[2] Subsequently, the cyclodimerizations of a variety vinylpyridines and vinylquinolines under similar conditions have also been established.[3]

Recently, a variety of intramolecular anion radical cyclobutanations of tethered bis(enones) have been described from these laboratories.[4] This work has looked at competitive anion radical chemical methods,[5] the scope, limitations and mechanisms involved,[6] and an intriguing diastereotopic electrolyte effect.[7]

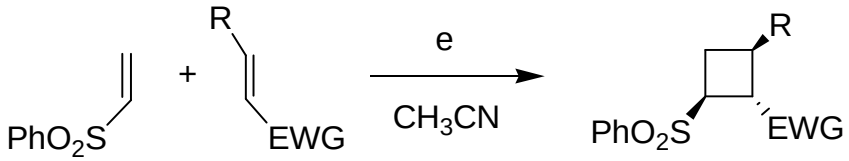
These three systems are of special interest because they represent the only published examples of inter- or intra-molecular anion radical cycloaddition, rather than the more common electrohydrocyclization/dimerization (EHC or EHD).[8] This chapter expands this field, into vinyl/ketone cross cyclization with phenyl vinyl sulfone.

This [2+2] cross cyclobutanation is assumed to proceed via anion radical to neutral substrate coupling, with rapid subsequent cyclization via a distonic anion

intermediate. This is based upon a complex electrochemical/computational study of the phenyl vinyl sulfone cyclodimerization,[9] and also the previous ability to trap the distonic anion radical of the analogous intramolcular enone case. [6]

IV-2. Cross cyclobutanations with phenyl vinyl sulfone

The well established electrocyclobutanation of phenyl vinyl sulfone was the starting point of this reseach thread, utilizing the idea that cross-cyclobutanation should be feasible with vinyl compounds containing electron withdrawing groups. While these vinyl compounds do not electrocyclobutanate, say due to polymerization, reaction with phenyl vinyl sulfone may prevent further reactivity, due the relative polymeric passivity of phenyl vinyl sulfone.



Scheme IV-1. Reactants involved in the cross-electrocyclobutanation reactions, where R = H, CH_3 and EWG = $COCH_3$, $COCH_3CH_2$, COPh, COPh-Ph.

While a large variety of substrates were studied, the only class of substrates that proved successful were ketonic. The yields are generally only modest (Table IV-1), and appear to be depressed by a variety of competing mechanisms. The cross-cyclobutanes formed are however entirely novel, and crystal structures of several are presented. While reactions are electrocatalytic in nature, the true extent of catalysis is not well defined, due to the competing mechanisms use of charge, the catalytic factors given are likely to be rather lower than those specifically engendered by the cross cyclobutanation. This is

particularly suggested by the more efficient cyclobutanation of phenyl vinyl sulfone alone, where a catalytic factor of around ten is quoted for a near quantitative reaction.[2,9] It is worth noting that the difficulty of repetition of this published result (by others who have attempted electrochemical syntheis, and by chemical reductive means) has lead to a degree of skeptism about the veracity of such a claim. I am able to confirm the published finding, with similar electrocatalysis values, and a yield in excess of 80% (the published quantitative yield requires a more complex experimental setup), and also provide crystallographic support for the E-1,2-diphenylsulfonecyclobutane product. Additionally reaction of tolyl vinyl sulfone has similarly been confirmed, with a cyclobutane yield over 70%.

Table IV-1. Summary of the yields and catalytic factors of cyclobutanes (**2**) formed from cross reaction of vinyl sulfones (**9b**, **9f**) with ketones (**9i** – **9w**)

Sulfone	Ketone	%Yield	Min. catalytic factor
9b: Phenyl vinyl	**9k**: 3-Penten-2-one	**2kb**: 26	5.7
9b: Phenyl vinyl	**9i**: Methyl vinyl ketone	**2ib**:28	4.9
9b: Phenyl vinyl	**9j**: Ethyl vinyl ketone	**2jb**: 32	8.9
9b: Phenyl vinyl	**9v**: Phenyl propenyl ketone	**2vb**: 45	1.7
9b: Phenyl vinyl	**9w**Biphenyl propenyl ketone	**2wb**: 28	5.7
9f: Divinyl	**9w**Biphe nyl propenyl ketone	**2wf**: 11	2.0

IV-2.1. 3-penten-2-one (**9k**).

The cross-cyclobutanation of 3-penten-2-one (**9k**) and phenyl vinyl sulfone (**9b**) occurs readily, to give **2kb** (Figure IV-1), in a variety of substrate ratio conditions, albeit in modest yields (Table IV-2). The nominal peak cross-cyclobutane yield occurs with a slight **9k** excess, although clearly there is no real variability in yield from a 3.5 fold **9k** excess to the reverse 3-fold **9b** excess. These results do not therefore suggest an appropriate route for yield improvement, and that a yield of around 25% may be maximal for this system. This could be due to the electroreactivity of **9k** under all conditions, such that oligomerization limits substrate availability. The formation of **2b-b**, from the dephenylsulfonylation of **2bb**, is a clear indicator of the presence of electrogenerated bases (EGB's). Indeed, added pro-bases, which form EGB's upon reduction, have been used to produce good yields of **2b-b (**Figure IV-2) from **2bb**.[10]

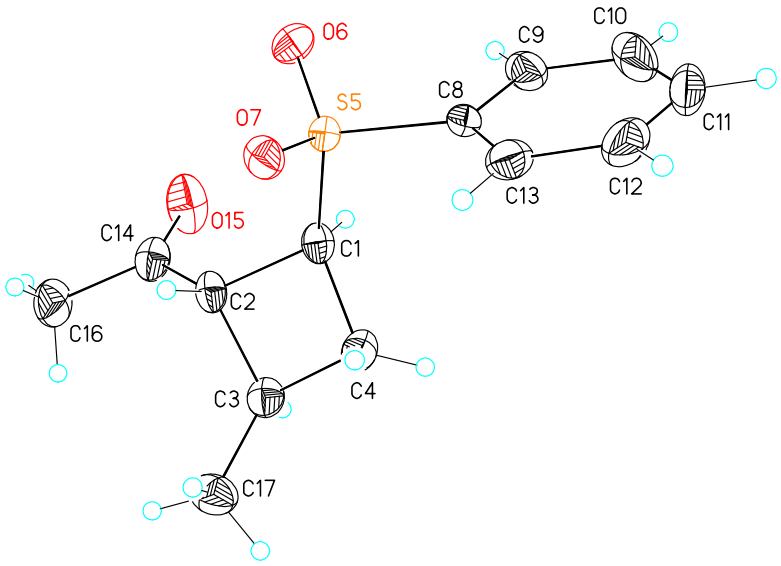


Figure IV-1. View of **2kb** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.

Table IV-2. The effect of substrate ratio upon cross-cyclobutanation reactions of 3-Penten-2-one (**9k**) with phenyl vinyl sulfone (**9b**).

9b:**9k**	Cross-CB %yield	Other products[a]	Catalytic factor
1:1.68	26	**2bb**:26% **2b-b**: ~3%	5.7
1:3.53	24	**2bb**: 21% **2b-b**: 14% **11kbb**: 4%	4.1
1.09:1	19	**2bb**, **2b-b**	3.2
3.02:1	22	**2bb**, **2b-b**	2.7

[a]Yields for products formed from **2b** (the cyclobutane **2bb**, and subsequent dephenylsulfonylation product, **2b-b**) are only given when **2b** is the limiting reagent.

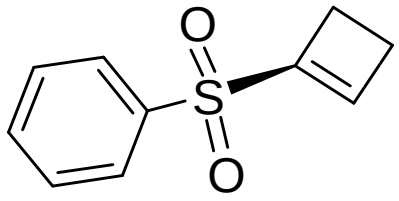


Figure IV-2. The dephenyl-sulfonylation product, **2b-b**, formed by EGB's from cyclobutane **2bb.**

IV-2.1. Methyl vinyl ketone (**9i**) and ethyl vinyl ketone (**9j**).

The reactions of two alkyl vinyl ketones with phenyl vinyl sulfone were also studied (Table IV-3). Unsurprisingly, the methyl and ethyl vinyl ketones behaved near identically, with cross-cyclobutane yields of around 30%. Increases in the excess of vinyl ketone clearly boost yield, although a 5-fold excess reaction actually led to no cyclobutane products, suggesting a limit to this approach, possibly due to the electropolymerization of the ketones. The greater catalytic factor for ethyl vinyl ketone, **9j**, may be a real, if inaccurately quantified, effect. The excess of phenyl vinyl sulfone readily dimerizes under these conditions (**2bb**), and leads to the formation of the EGB formed minor dephenylsulfonylation product, **2b-b**.

Table IV-3. The cross-cyclobutanation reactions of vinyl ketones (**9i** and **9j**) with phenyl vinyl sulfone (**9b**).

Substrate	**9b** excess	Cross-CB %yield	Other products	Catalytic factor
9i: Methyl vinyl ketone	1.84	14	**2bb**, **2b-b**	5.2
9i: Methyl vinyl ketone	2.89	28	**2bb**, **2b-b**	4.9
9j: Ethyl vinyl ketone	1.07	10	**2bb**, **2b-b**	11
9j: Ethyl vinyl ketone	2.90	32	**2bb**, **2b-b**	8.9

IV-2.1. Phenyl propenyl ketone (**9v**) and biphenyl propenyl ketone (**9w**).

The reactions of phenyl vinyl sulfone with phenyl propenyl ketone represent the best cross-cyclobutanation yield obtained, at 45%. It is thought that the reaction proceeds via reduction of **9v**, and subsequent addition to a neutral molecule of **9b**, due to the lower reduction potential of **9v** (appendix 1) and the observation that a 2:1 excess of **9v** over **9b** gave polymeric products. However, increasing the excess of **9b**, above two-fold, gives only a slight increase in cyclobutane yield (Table IV-4).

Table IV-4. The effect of ratio upon cross-cyclobutanation reactions of phenyl vinyl sulfone (**9b**) with aromatic propenyl ketones (**9v** and **9w**).

Substrate	**9b** excess	Cross-CB %yield	Other products	Catalytic factor
9v: Phenyl propenyl ketone	2.01	37	**2bb**, **2b-b**, **11vbb**	4.8
9v: Phenyl propenyl ketone	3.99	45	**2bb**, **2b-b**, **11vbb** (trace)	1.7
9w: Biphenyl propenyl ketone	4.00	28	**2bb** **11wbb, 15b**[a]	5.7

[a]Minor product, formed by **9b** reaction with solvent, discussed in chapter six.

The formation of minor amounts of the trimeric products **11vbb** and **11wbb** (Figure IV-3) are clear indication of competing EGB pathways in each electrolysis. This tentatively characterized minor product is thought to be formed via the EGB deprotonation of the propenyl ketone. The subsequent carbanion can then undergo sequential Michael additions to two moles of phenyl vinyl sulfone. This mechanism is entirely analogous to the rather more facile reactions observed for allyl phenyl sulfone, which are extensively explored in chapter five.

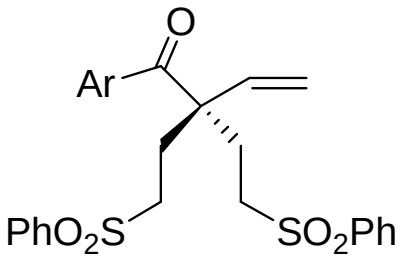


Figure IV-3. The trimeric product formed from carbanion addition to two moles of phenyl vinyl sulfone, **9b**.

11vbb: Ar = Ph, **11wbb**: Ar = Ph-Ph.

The reproducibility of the cross-cyclobutanation of biphenyl propenyl ketone is unfortunately in question. An initial suspect was a degree of moisture sensitivity, however this is far from certain. The formation of the trimeric **11wbb**, via EGB's, could feasibly be enhanced by the presence of water in the electrolyte solution. Extensive reactions were not considered time effective, particularly given the yields involved, and the failure of rigorous drying procedures to greatly reduce **11wbb** formation (reaction 3 in table IV-5). The 2:1 **9b** excess reaction was initially tried as the four-fold excess displayed limited **2bb** formation, suggesting that a lower ratio would be sufficient (and

simplify separation), whereupon reaction 1 gave no cyclobutane products. The additional drying steps, and care to use solvent immediately upon collection, did lead to some cyclobutanation, yet **11wbb** remained the primary product. While these results suggest moisture sensitivity, reaction 5 (table IV-5) does not fit this rationale well. The use of a 5:1 excess of **9b** should have given primarily cyclobutane, however, only small amounts were obtained (even by combining both cyclobutanes). This last reaction does at least suggest that this cross-cyclobutanation is somewhat reproducible, and that, with sufficient time, a suitable ratio could be arrived at to maximize cyclobutane yield.

Table IV-5. Summary of phenyl vinyl sulfone (**9b**) and biphenyl propenyl ketone (**9w**) reactions, evidence of moisture sensitivity?

Rxn	**9b** excess	Conditions[11]	% of charge	**2wb:2bb:11wbb**[a]
1	2.04	Raining, solvent not freshly collected[b]	24	**11wbb** only
2	2.04	Raining	10	1:0.2:5.1
3	2.00	No rain, electrolyte/substrates under vacuum for five hours	13	1:0.05:4.6
4	4.00[c]	No rain	12	1:0.2:0.3
5	5.01	No rain	19	1:0.5:1.1

[a]Ratio obtained from peak integration of crude product NMR.
[b]Solvent left in flask, septum and N_2 line attached, for apx. 6 hours.
[c]Reaction quoted in table IV-1.

IV-2.1. Divinyl sulfone (**9f**) and biphenyl propenyl ketone (**9w**).

The reaction between divinyl sulfone and biphenyl propenyl ketone, using a 4:1 excess of divinyl sulfone lead to a rather modest 12% yield (Table IV-1) of the cross-cyclobutane. While attempts to improve upon this yield were unsuccessful, this small yield does represent the only non-phenyl vinyl sulfone cyclobutanation obtained in this

work, although a vinyl sulfone moiety is still involved. A number of follow-up electrolyses have been run with excesses of other substrates along with **9w**, such as with vinyl ketones (**9i** and **9j**), and phenyl vinyl sulfone (**9b**), without successful formation of either a cyclobutane, or a trimeric 1:2 product.

IV-3. Other intermolecular cyclobutanation attempts

A rather extensive array of compounds were tested for their ability to electroreductively cyclobutanate, generally focusing upon vinyl compounds attached to electronwithdrawing groups. This would increase the lifetime of any anion radical formed, in the hope that an anion radical to neutral substrate coupling could occur. Other compounds with terminal vinyl groups were also attempted in cross reactions with phenyl vinyl sulfone, where these compunds could act as the neutral molecule for the phenyl vinyl sulfone anion to react with.

Initial study of cross-reactions with ethyl and methyl vinyl sulfone showed some promise, analysis of the crude products displayed NMR peaks in line with a cyclobutane product, and mass spectroscopy data showed a similarly consistant peak. However, separation proved problematic, as indeed it has with all products based upon these alkyl vinyl sulfones, which are thought to strongly adsorb to silica. When a single product is formed different procedures can readily be employed to obtain the product (as is done in chapters five and six), these procedures are not available in this case. Perhaps time will allow the development of a different separation procedure to access these assumed cross-cyclobutanes. With a four-fold excess of the alkyl vinyl sulfone yields were likely rather

low, based upon crude product NMR. Self-cyclobutanation of these alkyl sulfones does not occur due to competing reactions, discussed in chapter six.

Cyclobutanation was considered rather unlikely between propenyl compounds, for steric reasons, so was not extensively studied. However, electrolysis of phenyl propenyl ketone, **9v**, did give a modest 23% yield of an interesting EGB promoted product. This product, **10vv**, is once again formed via EGB deprotonation of the substrate to give a carbanion, which then adds to another mole of substrate, effectively giving a dimer. Again, this mechanism is entirely analogous to the self addition reaction observed for allyl phenyl sulfone, which is extensively explored in chapter five.

In concert with the electrolyte variation reactions examined in chapter three, several reactions were attempted using phenyl vinyl sulfone and perchlorate electrolytes. The only electrolyte to engender a reaction was potassium perchlorate, which was noted for its loose ion pairing in chapter three. The reaction was however far from competitive with the yet more loosely ion paired alkylammonium electrolytes. The reaction was run for approximately a fifth of the required charge, with only a small amount of the substrate converted to the cyclobutane, with noticeable amounts of **2b-b** already forming. It is unsurprising that strong ion pairing of other metal anions would inhibit intermolecular cyclobutanation, by simply blocking anion to neutral substrate approach.

Attempts to repeat the published 2- and 4-vinylpyridine electroreductive cyclobutanations[3] have proved wholely unsuccesful. While a variety of approaches have been attempted, such as varying electroylsis potentials, amounts of charge, electrolytes, and solvents, only one reaction (with magnesium perchlorate) showed the barest trace of a cyclobutane. The published work, which includes crystallographic support, utilizes a

mercury pool cathode, which was not available. It may be the case that this reaction is particularly sensitive to purity issues, such as the solvent, electrolyte and reactant. Cross reactions were attempted with phenyl vinyl sulfone, both in excess and as the limiting reagent, without indication of cross-cyclobutanation.

The following is a selection of compounds examined, the majority were electrolyzed in isolation, in many cases with both Et_4NBF_4 and $LiClO_4$, but all were co-reduced in a two-fold excess to phenyl vinyl sulfone (using Et_4NBF_4): acrylonitrile, methyl acrylonitrile, crotononitrile, methyl acrylate, ethyl acrylate, phenyl acrylate, methyl crotonate, ethyl crotonate, diethyl maleate, diethyl fumarate, dimethyl maleate, dimethyl fumarate, phenyl vinyl sulfoxide, diethoxy vinyl phosphonate, diphenyl vinyl phosphonate, phenyl vinylsulfonate, phenyl *trans*-styrl sulfone, 2-vinylpyridine, 4-vinylpyridine, 9-vinylanthracene, 1-vinylnaphthalene, 2-vinylnaphthalene, 1,3-cyclohexadiene, 2-cyclopenten-1-one, allyl phenyl sulfide, ally phenyl ether, 3-chloro-4,4,4-trifluoro-2-butenyl phenyl sulphone, 4-vinylanisole, 1-vinylimidazole, 9-vinylcarbazole, vinyl acetate, isoprene, norbornene, vinyl aldehyde, vinyl cinnamate, vinyl triethoxysilane, vinyl methacrylate, 3-methyl-2-cyclohexen-1-one, 1-acetyl-1-cyclohexene, 1-phenylsulfonyl-1,3-cyclohexadiene, 1,2-dichloroethene, diethyl ethylidenemalonate, 2-pentene, 4-methyl-5-vinylthiazole, butadiene sulfone, *trans*-cinnamonitrile, 4,4-dimethyl-2-cyclohexen-1-one, diphenyl alkyne, and vinyl ferrocene.

Conclusions

This cross-reaction approach has lead to modest to reasonable yields of entirely novel ketonic/sulfonyl cyclobutanes. These compounds have been electrocatalytically synthesized. There is not a readily competitive, single step, synthetic approach for this sub-class of compounds. While this synthetic method is far from universal applicability, the limited range does point toward future avenues of interest. This could include, but is not limited to, use of more complex ketone compounds, which retain the reactive vinyl/propenyl moiety on one side of the carbonyl, while the other side could be varied amoungst both aroyl and alkyl species. The presence, possibly unavoidable, of electrogenerated bases in these reactions is also confirmed.

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CHAPTER V

Electrogenerated base promoted addition reactions of allyl phenyl sulfone to electron deficient alkenes

V-1. Introduction

The buildup of basicity around the cathode during an electrolytic reduction has long been known. The use of such electrogenerated bases (EGB's) in directed synthesis has been investigated over the last few decades.[1] A prominent example of this phenomenon is the production of sodium hydroxide by electrolysis of water.[2] The applications of EGB's include the electro-activation of both C-H and N-H bonds, with subsequent N-C and C-C bond formation.[3,4] The typical approach has been to provide (usually in stoichiometric amount) an additive (called a pro-base)[5,6] which serves as a precursor to the active base. A relatively novel aspect of the reactions presented here is that, in contrast to most of the earlier applications of EGB's to organic synthesis, one of the reactants (allyl phenyl sulfone) also serves as the pro-base. This use of direct reduction of organic *acids* is an attractive, simplified approach, which can be utilized in two ways. Firstly, an *ex-situ* route, which is often enforced due to competitive substrate reduction.[7] Secondly, and rather rarely, an *in situ* route as presented here. This approach sees a further layer of experimental simplification, and has been utilized for malonic acid derivatives, for example.[8]

The reactive EGB's formed during reduction lead to exceptionally efficient and highly electrocatalytic additions of allyl phenyl sulfone (*via* its conjugate base) to a

variety of vinyl and propenyl compounds, in which these groups are attached to electron withdrawing groups (sulfone, ketone, nitrile, and ester).

The first Bauld group publication[9] in this area showcased EGB promoted addition of allyl phenyl sulfone carbanion to its propenyl isomer, along with its novel reactions with vinyl sulfones to furnish high (90-94%) yields of highly polar molecules. Where one mole of allyl phenyl sulfone has added consecutively, selectively, and in a linear addition mode to two moles of the vinyl sulfone.

The follow up full publication[10] initially expands the scope of this Michael addition to include other vinyl sulfones, obtaining similarly high yields. Competitive addition to two different vinyl sulfones is also examined, allowing for incorporation of a mole each of two sulfones. An attempt has also been made to probe the range of electron-deficient substrates (ketone, nitrile and ester) that will allow Michael addition of the electrogenerated[11] conjugate base of allyl phenyl sulfone. The formation of 1:2 adducts (**11**) is seen to be generally limited to vinyl compounds (Figure V-1). The formation of 1:1 adducts (**10**) is mostly seen with propenyl substrates. However, several vinyl compounds yield both product types, the ratio between which is explored, and a mechanism is advanced. A large variety of terminal vinyl group containing compounds were also explored as possible substrates, the lack of success of this approach is clear indication of a need for an electron withdrawing group, and is discussed in terms of the scope of this reaction.

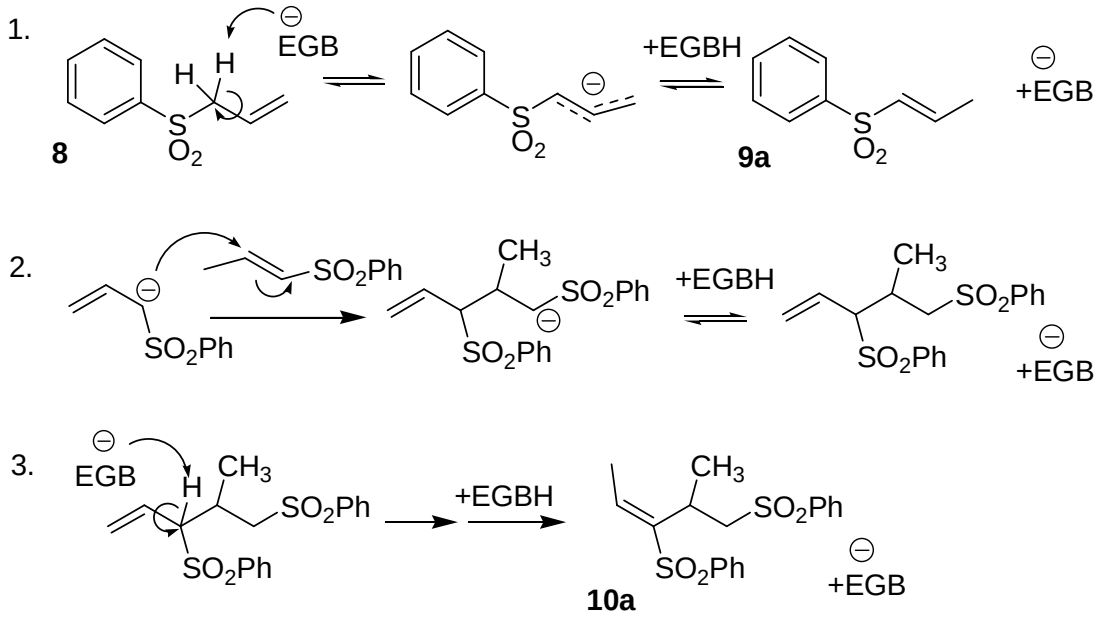
The coupling of simple alkyl groups at the α position of allyl phenyl sulfone has previously been seen (in a two step chemical synthesis).[12] However, the present work represents a large increase in the range of moieties that will couple at the reactive α

position. Stoichiometric use of strong bases has been used in related allylic sulfone compounds to affect addition to α,β-unsaturated esters,[13] cyclic ketones and nitroalkenes.[14] The conjugate base of the allyl sulfone was produced in a non-electrochemical manner in these latter cases. The environmentally benign nature of this work's electrochemical formation of the reactive carbanion, inherent in the simplified workup and the consumption of electricity as the sole reagent (in catalytic amounts), further adds to the experimental appeal and potential utility of these reactions.

V-2. "Dimerization" of Allyl Phenyl Sulfone.

In the initial phase of this research, the reactivity of the EGB formed under our electrochemical conditions and the efficiency of base-catalyzed Michael-type additions under such conditions, was demonstrated in a study of the self-addition of allyl phenyl sulfone (**8**). This reaction was found to afford the dimer **10a** in 81% yield, with a catalytic factor of at least 11 (equivalent to a 0.087 F mol^{-1} process). This same dimer has been reported in the literature[15] in one other instance, as a product of a cathodic reduction of the isomeric molecule phenyl *trans*-propenyl sulfone, a substrate which would furnish the same conjugate base as allyl phenyl sulfone. In that study, the yield of **10a** obtained was only 56% (catalytic factor of at least 10). Further, an anion radical mechanism was proposed for the formation of **10a,** which we consider inconsistent with typical anion radical behavior. Rather, the base-catalyzed Michael-type addition illustrated in Scheme 1 is presently proposed. Such an electrogenerated base promoted mechanism has previously been advanced for the electrocatlyzed self addition of 2-cyclohexen-1-one.[11,16]

The mechanism of generation of the EGB is by no means certain, but appears to involve the initial reduction of **8** to the corresponding anion radical. It is possible that this anion radical is itself the EGB, which initiates the deprotonation of **8**. Alternatively, the anion radical may deprotonate solvent/electrolyte molecules, forming a base which deprotonates the allyl phenyl sulfone in solution. Interestingly, the structure of the dimeric product reveals that the conjugate base adds not to the unactivated double bond of **8**, but to the activated, electron deficient double bond of its position isomer, phenyl propenyl sulfone (**9a**), which would be produced by a rapid, base-catalyzed equilibration of **8** and **9a** (step 1 of Scheme V-1). The latter isomer has in fact been detected (NMR) in these reacting solutions. The addition of the conjugate base of **8** to the α position of **9a** yields a dimer carbanion, which is subsequently protonated either by **8**, to yield more conjugate base, or by the conjugate acid of the EGB, to regenerate the EGB. It is noted that the protonation of the dimer carbanion by **8** should be exergonic, since the latter carbanion has a greater degree of delocalization. Finally, the double bond of the initially produced dimer undergoes base-catalyzed position isomerization (step 3 of Scheme 1). The final product, **10a**, was shown using nOe to have a trans methyl group to the sulfonyl, as shown in the scheme, rather than the earlier reported cis conformation.[15] It is of interest that subjection of **8** to typical base catalysis conditions yields no detectable amount of "dimer" **10a**, but rather produces various oligomers and condensation products. These base conditions while not exhaustive included ^{t}BuOK in ^{t}BuOH, and ^{t}BuOK in DMSO, at varied temperatures, for different lengths of time.

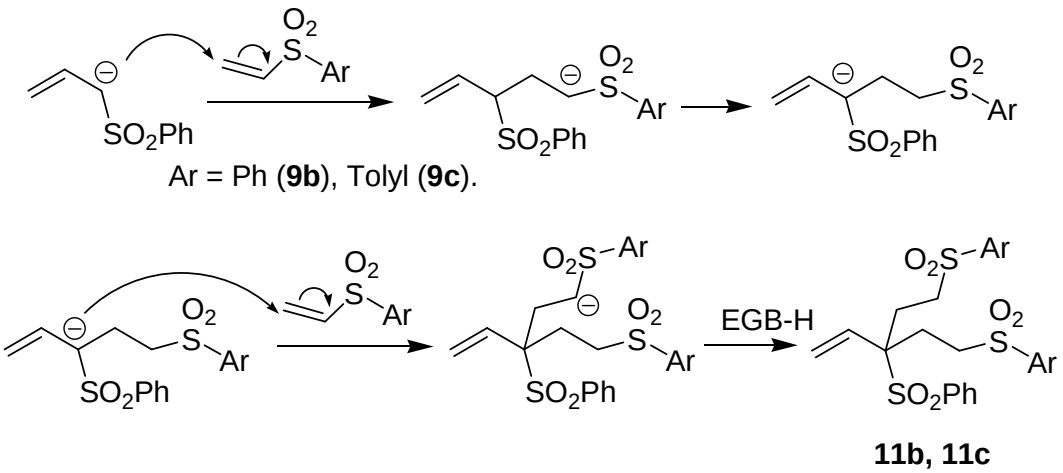


SchemeV-1. Mechanism of ele ctrogenerated base-catalyzed "dimerization" of allyl phenyl sulfone, to form the self adduct **10a**.

V-3. Initial additions to electron deficient vinyl substrates.

In view of the observation that the conjugate base of **8** undergoes efficient conjugate addition to phenyl propenyl sulfone, it appeared likely that cross additions to vinyl sulfones, might be even more efficient. Such vinyl sulfones would not be susceptible to deprotonation, so that they could not fulfill the carbanion role but could serve as ideal Michael acceptors. However, a plausible possibility was that additions of the conjugate base of **8** to these receptors might generate a mixture of dimers, trimers, oligomers, and even higher polymers.

The addition reactions of **8** with phenyl and tolyl vinyl sulfone (substrates **9b** and **9c**) under our conditions somewhat surprisingly lead to quite high yields of single compounds, which are not dimers, but trimers, in which the conjugate base of **8** has added to two and only two molecules of the receptor. Further, even when a 2.06:1 ratio of receptor to **8** is used, the "trimers" are generated cleanly and in high yield, unaccompanied by any formation of **10a**. The proposed general mechanism for the formation of these linear trimers is given in Scheme V-2. Preferential addition of the conjugate base of **8** to the vinyl sulfone component as opposed to the propenyl sulfone is expected based not only upon steric effects, which are minimal in the case of the vinyl sulfone, but also because of the concentration of **9a** never rises to a very high level in these solutions (presumably <2% of the mixture of **8** and **9a)**. The addition of the dimer carbanion to another mole of the vinyl sulfone then follows rapidly and equally selectively, leading to a trimer carbanion. Interestingly, these reactions do not form significant amounts of tetramers, oligomers or polymers, so that there is no apparent tendency of this latter carbanion to add to any further molecules of the vinyl sulfone. It appears reasonable to propose that the pronounced difference in nucleophilic reactivity between the trimer carbanion and the dimer carbanion is the result of increased steric hindrance at the carbanion site of the trimer.



SchemeV-2. Mechanism of electrogenerated base -catalyzed addition of allyl phenyl sulfone carbanion to vinyl compounds containing electron withdrawing groups. The initially observed additions to phenyl vinyl sulfone and tolyl vinyl sulfone are shown for example, with "trimer" or 1:2 product yields in excess of 90%.

V-4. Carbanion-mediated vs. anion radical mediated reaction mechanisms.

The isomerization of allyl phenyl sulfone to phenyl propenyl sulfone is required by the structure of the dimeric product obtained from the former sulfone. It appears logical, and even essential, to propose a base catalyzed mechanism for this isomerization, which would require the intermediacy of the common conjugate base of both sulfones. Since this conjugate base is obviously present in the reaction medium, and since the Michael addition of this base/nucleophile to electron deficient double bonds is readily observed, it appears likely that **8** is formed *via* an exclusively carbanion-mediated process. Incidentally, the final double bond isomerization also would appear to require a base catalyzed process. The formation of the specific trimers observed in the cross additions' also appears to be rather uniquely consistent with a carbanion mechanism. Further, the highly catalytic nature of these reactions is consistent with electrogenerated

base catalyzed chemistry. Such high catalytic factors have not been observed in the case of anion radical chemistry.[17-19] Still another relevant observation is that the anion radical of phenyl vinyl sulfone undergoes a rapid cyclobutadimerization reaction.[20] No such product is observed in the case of the cross addition of **8** to phenyl vinyl sulfone. Indeed, These results have been repeated in our group, with yields in excess of 80%, with the exact same cell, solution, electrolyte and reduction potentials as the reactions reported here (minus the presence of allyl phenyl sulfone).

Finally, the absence of anion radical pathways is further indicated by the observation that when the electrolyte is changed to lithium perchlorate, the dimerization of **8** does not proceed. No reaction is observed, even after the passage of several F mol^{-1}, yet this electrolyte is known to favor anion radical promoted cyclizations, whilst allowing at best limited base reactivity. Indeed, research in this group has established a complete suppression of competing EGB pathways in intramolecular anion radical mediated cycloadditions, when the electrolyte is changed from alkylammmonium salts to lithium perchlorate, as discussed in chapters two and three.

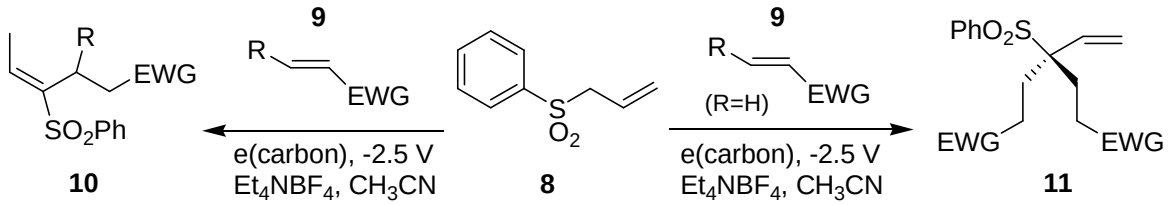


Figure V-1. Summary of the products formed from the addition of the carbanion of **8** to one or two moles of various vinyl/propenyl compounds containing electron withdrawing groups (EWG's).

Table V-1. The yields and structures of primary products formed from the addition of the carbanion of **8** to one or two moles of various vinyl/propenyl compounds containing electron withdrawing groups (EWG's).

Substrate **9**	R	EWG	Primary product/Yield (%)
9a	CH_3	$PhSO_2$	**10a**: 81
9b	H	$PhSO_2$	**11b**: 91
9c	H	CH_3PhSO_2	**11c**: 95
9d	H	$CH_2CH_3SO_2$	**11d**: 96
9e	H	CH_3SO_2	**11e**: 92
9g	H	CN	**11g**: 57
9h	CH_3	CN	**10h**: 26
9i	H	$COCH_3$	**10i**: 28
9j	H	$COCH_2CH_3$	**10j**: 47
9k	CH_3	$COCH_3$	**10k**: 26
9l	H	$COOCH_3$	**10l**: 16 **11l**: 18
9m	H	$COOCH_2CH_3$	**10m**: 28 **11m**: 20
9n	H	COOPh	**10n**: 22
9o	CH_3	$COOCH_3$	**10o**: 6
9p	CH_3	$COOCH_2CH_3$	**10p**: 6
9q	$COOCH_2CH_3$	$COOCH_2CH_3$	**10q**: 22

V-5. Bis addition to vinyl sulfones.

Consequently, the expansion of this work to other vinyl sulfones: using ethyl and methyl vinyl sulfone (**9d** and **9e**) as electron-deficient addends unsurprisingly followed a similar pattern of forming high yields of the trimer product, **11** (Table V-2).

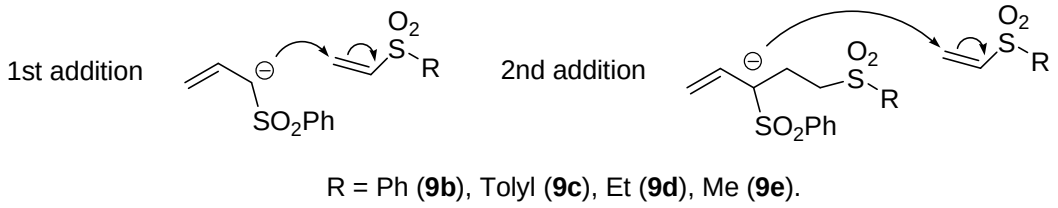
Table V-2. Yields and minimum catalytic factors for cross addition of allyl phenyl sulfone to electron deficient alkenes, leading to exclusive trimer formation.

Substrate	Yield (%)	Min. catalytic factor
9b: Phenyl vinyl sulfone	91	13
9c: Tolyl vinyl sulfone	95	7.4
9d: Ethyl vinyl sulfone	96	17
9e: Methyl vinyl sulfone	92	15

These trimers were all produced from reactions with a vinyl sulfone excess of <2.10, over **8**. Indeed when the reaction is run using an excess of **8** at a 1.97:1 ratio (to **9b**), only the trimer (**11b**) and the allyl phenyl sulfone carbanion addition to propenyl phenyl sulfone (**9a**) product (**10a**) are obtained. These products are seen in a 1:1.45 ratio, respectively, in accord with the proposal that exclusive trimer formation occurs until the vinyl substrate is largely consumed, followed by self-addition of the excess **8.** A **8**:**9b** ratio of 1:2 using theses assumptions, should yield a 1:1.5 **9a** excess.

The trimers formed from addition of **8** to vinyl sulfones form readily in near quantitative yields. The reactions also utilize all of the vinyl sulfone substrate prior to formation of **10a**, so that the reactivity of the allyl carbanion to each vinyl sulfone substrate can be probed by competitive addition with two substrates in the reaction. The excess of any one substrate was kept insufficient (below 2) to allow complete reaction

with that substrate only. In this way, each reaction yields three trimers, two based on the addition to two moles of each vinyl sulfone, along with a "mixed" trimer containing one mole of each vinyl sulfone. The reactivities of the vinyl sulfones (based on product ratios in Table V-3) generally follow a pattern which is consistent with the expected relative stabilities of the α-sulfonyl carbanions which would be formed in the nucleophilic addition steps, based upon the relative inductive effects of the four substituents attached to the sulfonyl group (phenyl, tolyl, ethyl, and methyl. Presumably these effects are present in both addition steps (see Figure V-2). These mixed reactions show a reactive rank of **9b**>**9c**>**9d**>**9e**, as judged by the relative amounts of the two 1:2 adducts (the first and third numbers in the product ratios).



R = Ph (**9b**), Tolyl (**9c**), Et (**9d**), Me (**9e**).

Figure V-2. A portion of the reaction mechanism for bis addition (scheme V-1).

Table V-3. Reactions of allyl phenyl sulfone, **8**, with two vinyl sulfones to yield "mixed" trimers (1:2 products) incorporating all three components. A sample mixed trimer is shown in Figure V-3.

Substrates	Starting ratio where **8** = 1	Products	Product ratio[a]
9b + **9d**	1.52:1.48	**11d**:**11bd** **11b**	1:3.22:3.42
9c + **9d**	1.50:1.52	**11d**:**11cd**:**11c**	1:2.80:2.30
9c + **9d**	1.01:1.20	**11d**:**11cd**:**11c**	1:1.54:0.77
9b + **9e**	1.51:1.65	**11e**:**11be**:**11b**	1:2.73:2.69
9d + **9e**	1.62:1.60	**11e**:**11de**:**11d**	1:2.03:1.15[b]

[a]Based upon NMR integration of vinyl protons.
[b]Based upon LRMS, as vinyl proton NMR were coincident.

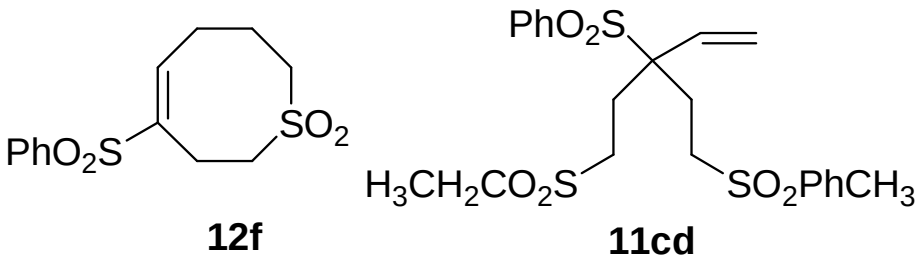


Figure V-3. The cyclic 1:1 product, **12f**, formed from α,γ-addition of allyl phenyl sulfone (**8)** to divinyl sulfone (**9f)**. An example of a mixed trimer, **11cd**, formed from addition of **8** to one mole each of tolyl vinyl sulfone (**9c**) and ethyl vinyl sulfone (**9d**).

V-6. Formation of 1-Phenylsulfonyl-5-thia-5,5-dioxycyclohept-1-ene.

The reaction of **8** with **9f** gives a rather unexpected and novel product, the eight-membered ring product **12f** (Figures V-3 and V-4). The yield of this product (41%) is more modest than those observed in the previously described vinyl sulfonyl additions, but the coupling of the conjugate base of allyl phenyl sulfone once at the position α to the phenylsulfonyl group and then again γ to it, to yield an eight-membered ring is rather novel. As in the previously described reactions, coupling undoubtedly occurs first at the α position, followed rapidly by intramolecular addition from the γ position (Scheme V-3). Presumably, the preference for reaction at the γ position to give a cyclooctene derivative over addition from the α position, to give an eight-membered ring product derives from the circumstance that the α carbon is now tertiary, and much more highly hindered than the γ carbon, which is primary.

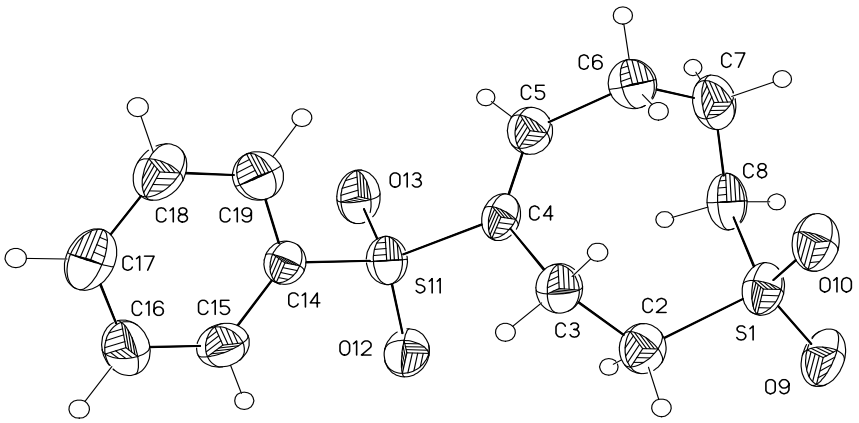
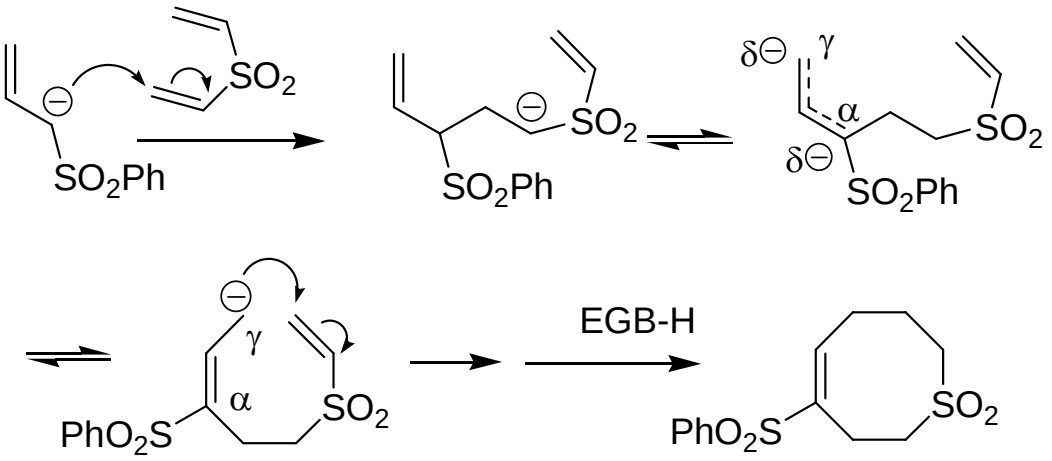


Figure V-4. View of 1-Phenylsulfonyl-5-thia 5,5-dioxycyclohept-1-ene (**12f**) showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.

There is no higher order oligomer (such as trimer) formation, such as would be expected if the ring closure step were slower than addition to another molecule of **9f**. Presumably the intramolecularity of the cyclization process provides the basis for the kinetic preference for cyclization over oligomerization. The maximized yield given above is obtained when the ratio of **9f** to **8** is greater than 3:1. In contrast to the other reactions, unreacted **8** is generally recovered from this cyclization. When the ratio of **9f** to **8** is less than 3:1, the formation of some **10a** is also observed. The mechanistic formation and structural novelty of this 8-membered thia-ring has been commented upon (favorably) by publication referees and presentation attendees on a number of occasions.



SchemeV-3. Proposed mechanism for the α, γ position addition/cyclization of allyl phenyl sulfone carbanion to divinylsulfone, to give the eight-membered thia-ring: 1-phenylsulfonyl-5-thia 5,5-dioxycyclohept-1-ene (**12f**).

V-7 Addition to vinyl/propenyl nitriles.

The addition to a vinyl nitrile (**9g**, acrylonitrile) gave reasonable yields of products consisting primarily of the 1:2 adduct (Table V-4). The competing formation of the monoadduct can be suppressed by using a slightly higher excess of **9g**. Under these conditions the yield of the trimer, **11g**, is increased to 57%.

Table V-4. Product yields for the addition of **8** to a vinyl and a propenyl nitrile.

Substrate	Substrate excess (**8**=1)	% Yield of 1:1 product (**10**)	% Yield of 1:2 product (**11**)	% Yield of other products	Min. catalytic factor
9g: Acrylonitrile	2.06	6	42	**9a**: 3	25
9g: Acrylonitrile	3.09	-	57	-	12
9h: Crotononitrile	3.11	26	-	**10a**: 43	16
9h: Crotononitrile	5.98	22	-	**10a**: 28	12

Addition to a propenyl nitrile (**9h**, crotononitrile) is seen to be less facile, with yields of the 1:1 product of ca. 25%. The 1:2 adduct is not observed, and indeed the yield of the 1:1 adduct is not increased by using a greater excess of **9h**, even though the yield of the self adduct of **8** (**10a**) is diminished. This is probably due to greater competition from oligomerization reactions engendered by the excess of **9h**.

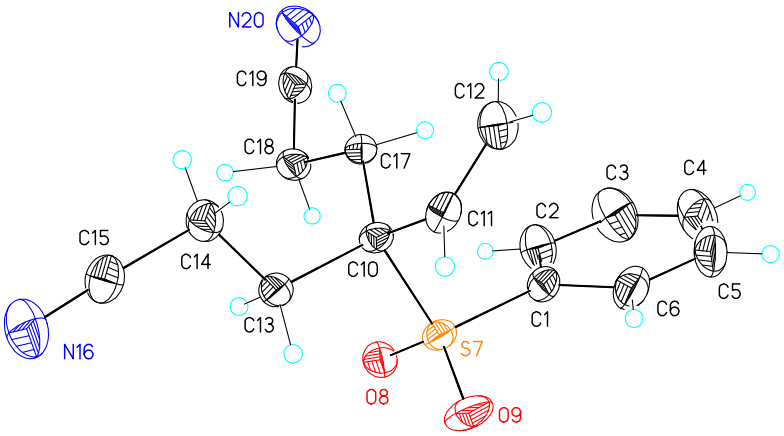


Figure V-5. View of **11g** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.

V-8 Addition to vinyl/propenyl ketones.

The addition to a series of vinyl/propenyl ketones leads to reasonable yields of 1:1 adducts, approaching 50% in the case of ethyl vinyl ketone (Table V-5). Yields of 2:1 products are relatively limited (and not seen for **9k**). A secondary reaction of the formed trimers, **11i** and **11j**, leads to an additional product; **13**. This product is formed via an aldol-type cyclization,[19] shown in scheme V-4. However, both products **11i** and **13i** are formed in low yields even when the ratio of methyl vinyl ketone (**9i**) is trebled, leaving the 1:1 dimer as the main product. The near four-fold excess of ethyl vinyl ketone does

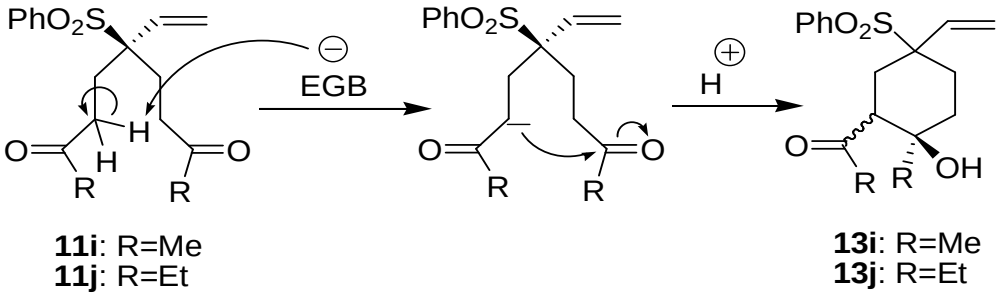
not lead to large yields of **11j** or **13j**, indicating a distinct preference to form the dimer **10j**. It appears that addition to a second mole of ketone is less favored in the ethyl vinyl ketone case. The rationale for this may be steric in nature, or involve the slight differences in acidity of the substrates. An additional curiosity was observed, that use of an old supply of ~90% tech grade methyl vinyl ketone lead to a 45% yield of the 1:1 product (along with 7% of **9a**), presumably the impurities are acidic in nature, protonating the intermediate after one addition. Introduction of small amounts of water, and acetic acid, into pure **9i** electrolyses, however, did not re-create these results.

Table V-5. Product yields for the addition of **8** to a series of vinyl and a propenyl ketones.

Substrate	Substrate excess (**8**=1)	% Yield of 1:1 product (**10**)	% Yield of 1:2 derived product	% Yield of other products	Min. catalytic factor
9i: Methyl vinyl ketone	1:1.00	28	**13i**: 5[a]	**9a**: 7 **10a**: 6	13
9i: Methyl vinyl ketone	1:3.05	18	**13i**: 12[a]	-	11
9j: Ethyl vinyl ketone	1:2.01	27	**13j**: trace	**9a**: 1	6.7
9j: Ethyl vinyl ketone	1:3.84	47	**13j**: trace	-	7.9
9k: Propenyl methyl ketone	1:2.52	26	-	**10a**: ~ 4	4.2

[a]Two isomers, see experimental chapter for details

Addition to the propenyl ketone studied, **9k**, led to moderate amounts of the 1:1 dimer, the presence of the propenyl group clearly retarding trimer formation. Increases in the excess of **9k** actually reduced yields, at 6:1 no **10k** was formed. This is clearly due to the reactivity of the ketone under these conditions, probably leading to a variety of oligomerization reactions. This reactivity is also indicated by the lowered catalytic factor, as some of the charge is used by the ketone. Indeed the ketone is seen to undergo a low yield "dimerization" thought to proceed via a similar carbanion formation (followed by addition to the propenyl ketone) mechanism as shown in Scheme 1, for allyl phenyl sulfone. This is discussed further in section VII-2.



11i: R=Me
11j: R=Et

13i: R=Me
13j: R=Et

SchemeV-4. Formation of **13** via aldol-type cyclization of **11**.

V-9. Addition to vinyl esters.

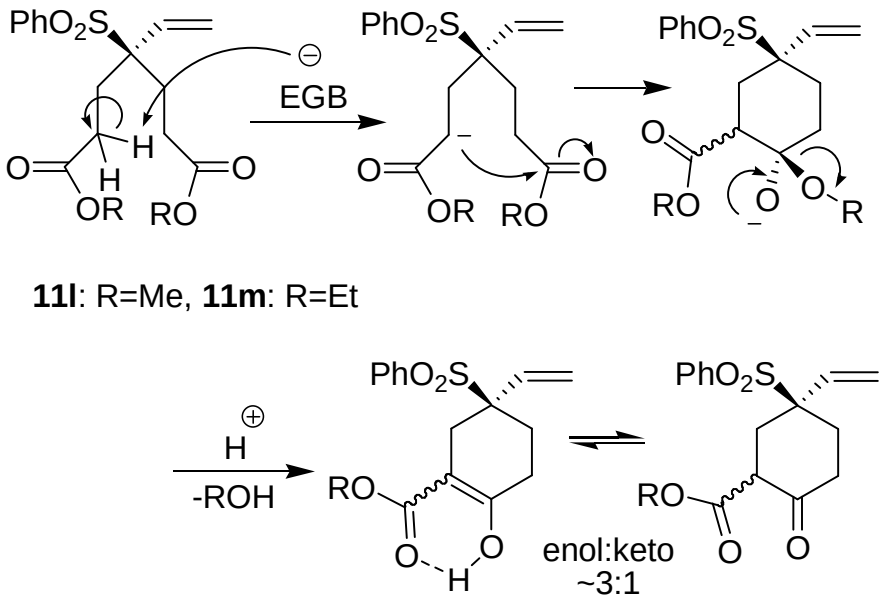
The coupling of the allyl phenyl sulfone carbanion to a series of esters yielded both adduct types (1:1 and 1:2) along with the formation of a third product derived from the 1:2 trimer. The catalytic factors seen in all three additions are some of the lowest observed in this work, this taken with the moderate yields, indicates reduction and possible reactivity of the substrates themselves (say, via oligomerization). Addition to methyl and ethyl acrylate generally proceeded to reasonable total product yields around 50% (Table V-6). As noted, this yield is made up of three products, with **14** being formed from the cyclization of **11**, and subsequent condensation (loss of an alcohol).

Table V-6. Product yields for the addition of **8** to a series of vinyl esters.

Substrate	Substrate excess (**8**=1)	% Yield of 1:1 product (**10**)	% Yield of 1:2 product (**11**)	% Yield of other products	Min. catalytic factor
9l: Methyl acrylate	2.09	16	18	**9a**: 8 **14l**: 12	2.5
9m: Ethyl acrylate	2.09	28	20	**9a**: 8 **10a**: 3 **14m**: 7	4.5
9m: Ethyl acrylate	3.08	13	15	**9a**: 2 **14m**: 13	2.0
9n: Phenyl acrylate	2.03	22	-	**9a**: 24	1.5

An attempt was made to force the reaction all the way to this cyclic product by increasing the excess (in this case, of ethyl acrylate), and reducing for longer. While **9a** formation is reduced, and no **8** is recovered, there is still some formation of the 1:1 adduct. The yield of the cyclic product is somewhat increased, at the expense of total product yield. This cyclic product is a keto-enol tautomer, with the enol form

predominant in ca. 3:1 excess (in d-chloroform), while x-ray crystallography shows only the enol form (see Figure V-6). The mechanism for formation of **14** is presented in Scheme V-5.



Scheme V-5. Formation of the keto-enol tautomer **14** via cyclization/ condensation (loss of alcohol, MeOH or EtOH).

The addition to phenyl acrylate, **9n**, interestingly stops at the 1:1 adduct stage. While this may in part be due to the steric hindrance of the more bulky phenyl group, it may also be appropriate to consider a possible additional electronic basis relating to the resonance interaction of the phenyl group with the attached ester oxygen. This interaction, which is not present in an alkyl ester, competes with normal ester resonance, making the oxygen atom bound to the phenyl group less electron donating than in the

case of an alkyl ester. The net result is that the ester carbonyl group is more electron-deficient than in the case of alkyl esters and better able to stabilize the intermediate carbanion. This would not only enhance the rate of the initial addition, but perhaps retard the rate of the second addition.

If we consider **14** to form via the trimer, we see that while equal amounts of **10m** and **11m** were formed in the electrolysis, there is a slight excess of **10l** formation over **11l** (30%:16% respectively). This observation, while small in magnitude, falls in line with the previous discussion, by considering ethyl acrylate a small step along the route from methyl acrylate to the extreme case of phenyl acrylate.

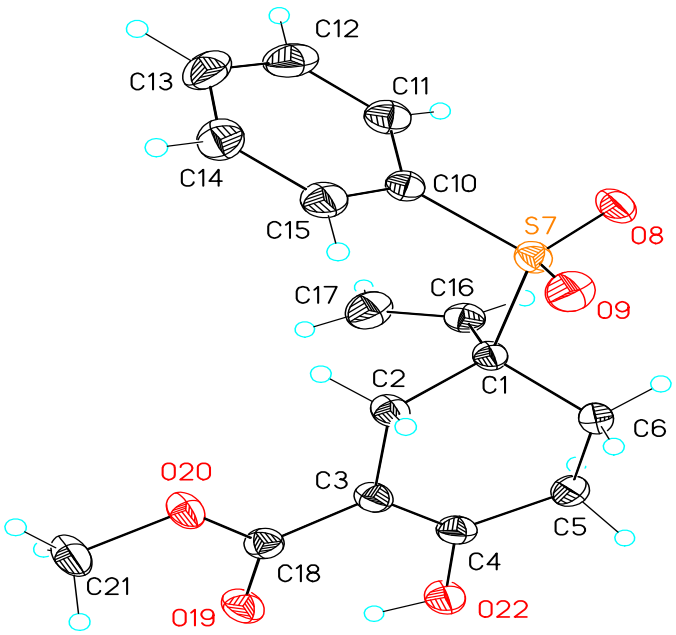


Figure V-6. View of **14l** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level

V-10. Addition to other esters.

The carbanion addition to propenyl esters is rather inefficient, leading to disappointing yields of the 1:1 cross addition product of just 6% in each case (Table V-7). It is clear from the reasonable yields of **10a** (ca. 50%) that the addition of the carbanion is much more facile to the *in situ* formed **9a** than to the higher concentration propenyl ester.

Table V-7. Product yields for the addition of **8** to varied esters.

Substrate	Substrate excess (**8**=1)	% Yield of 1:1 product (**10**)	% Yield of other products	Min. catalytic factor
9o: Methyl crotonate	2.00	6	**10a**: 57	11
9p: Ethyl crotonate	2.09	6	**10a**: 46	8.0
9q: Diethyl maleate	1.02	11	**9a**: 20 **10a**: 16	4.0
9q´: Diethyl fumarate	1.03	22	**9a**: 4	2.1

The addition of the allyl phenyl sulfone carbanion to diethyl maleate (**9q**) and diethyl fumarate (**9q´**) leads to formation of the same 1:1 adduct (**10q**). The reaction picture here is rather unclear, firstly it appears that additional reduction time for the fumarate doubled the yield of **10q** whilst restricting **9a** formation (presumably by consuming any that is formed). However continued reduction generally leads to limited product yields, indicating that the 1:1 adduct may itself be electroreductive under these conditions.[21] Also, increased excess of the maleate/fumarate does not improve yields, a 3:1 excess giving only trace amounts of the 1:1 product. This suggests that **9q**/**9q´** are reducing under these conditions, possibly leading to oligomerization. It may be the more advanced oligomerization in the reaction with the fumarate, inherent in greater reduction time, which consumes any **10a** that is formed. It seems unlikely that any difference in the

reactivity of the isomers would lead to formation of **10a** in one case and not the other, particularly as the same 1:1 adduct is formed in both cases.

V-11. Other additions.

There are a handful of further examples of EGB formed allyl phenyl sulfone carbanion addition reactions where time constraints have not allowed for a full determination of the success of the reaction. Addition to dimethyl maleate/fumarate, where there is indications of two 1:1 products, although yields are low, isolation proved problematic, and the reaction displayed substrate reduction complications akin to those observed for diethyl maleate/fumarate.

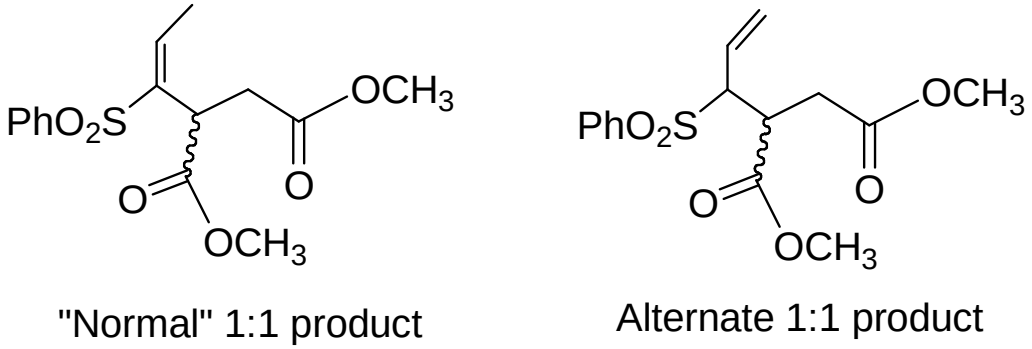


Figure V-7. Two 1:1 products formed from the reaction of **8** with dimethyl fumarate and dimethyl maleate, partial characterization is given in the experimenta l section.

Early indications do show a difference in the 1:1 product formed from the additions, namely that addition to dimethyl maleate gave the “normal” 1:1 product in apx. a 2.5:1 excess over what is thought to be another 1:1 product which differs in being allyl rather than propenyl. This ratio is more than reversed in the case of addition to dimethyl fumarate, where the allyl product is formed in apx. a 4:1 excess of the propenyl 1:1

product form. Presumably this is based upon a steric affect of the coupling of the allyl phenyl sulfone carbanion to one isomer, say the fumarate, such that the allyl moiety is sterically favored by keeping the double bond further from the clustered carbon center β to the sulfonyl. Additionally, this effect is not seen in the related diethyl system, perhaps a conformational argument can be made, but this appears difficult without further structural assignment. The hope is that future yield improvements (see section VI-2) will lead to improved purity and subsequent crystallographic assistance.

Addition to methyl acrylonitrile lead to a reasonable yield of a 1:1 product, presumably around 20%, along with about twice that yield of the self adduct **10a**. Substrate excess optimization/yield maximization has yet to be completed, although it is clearly unsurprising that there is no indication of a 1:2 product (analogous to the reasonable yield 1:2 product obtained from addition to acrylonitrile), given the added hinderence of the methyl group. Similar reactivity is seen with addition to propenyl biphenyl ketone, a 1:1 product is clearly formed along with **10a**, amoungst other unidentified products. Addition to a cyclic ketone (2-cyclopenten-1-one) also lead to a 1:1 product (unlikely to be greater than 20% yield) along with a similar yield of the isomer propenyl phenyl sulfone, **9a**. Addition to the related 2-cyclohexen-1-one did not proceed, due to the EGB promoted self addition of the substrate. It appears that this previously published[11,16] dimerization is too facile for cross reaction, either via the carbanion of the substrate adding to *in situ* formed propenyl phenyl sulfone, or the reverse allyl phenyl sulfone carbanion adding to the 2-cyclohexen-1-one. The first possibility is probably hampered by the low concentration of **9a** during reaction, while the lack of success of the second possibility indicates that the 2-cyclohexen-1-one is

preferentially reducing, and that its reduction to the anion is the true EGB in solution. The 2-cyclohexen-1-one appears to be entirely consumed (yielding primarily the dimer) before any self-addition of ally phenyl sulfone occurs. Indeed, there have been previous attempts to electrolytically Michael cross react 2-cyclohexen-1-one (with a β-keto ester), where cross reaction only occurred after the 2-cyclohexen-1-one had dimerized.[22]

In these cases, a substrate excess of 2-3 was used, with an additional study with a ten-fold excess of 2-cyclohexen-1-one (in an attempt to force allyl phenyl sulfone carbanion addition to the 2-cyclohexen-1-one). Full yield analysis was hampered by purification problems, although tentative product determination is based upon ^{1}H NMR of impure samples, namely quartet peaks at around 7 ppm (for 1:1 products). Further details of these reactions are outlined in the experimental section, along with partial product characterizations.

A plethora of further substrates were attempted, in general the self addition of the allyl phenyl sulfone carbanion to the *in situ* formed propenyl isomer was too facile to allow for any competition. In these cases **10a** was formed in reasonable to good yields, while much of the substrate was recovered unreacted. In a number of cases, substrate reactivity in the form of polymerization, was observed. Such that no unreacted substrate was recovered, and generally allyl phenyl sulfone "dimerization" was supressed. Substrates attempted were not limited to vinyl compounds containing electron withdrawing groups, they include: phenyl vinyl sulfoxide, diethoxy vinyl phosphonate, diphenyl vinyl phosphonate, phenyl vinylsulfonate, phenyl *trans*-styrl sulfone, 2-vinylpyridine, 4-vinylpyridine, 9-vinylanthracene, 1-vinylnaphthalene, 2-vinylnaphthalene, 1,3-cyclohexadiene, allyl phenyl sulfide, ally phenyl ether, 3-chloro-

4,4,4-trifluoro-2-butenyl phenyl sulphone, 4-vinylanisole, 1-vinylimidazole, 9-vinylcarbazole, vinyl acetate, isoprene, norbornene, vinyl aldehyde, vinyl cinnamate, vinyl triethoxysilane, vinyl methacrylate, 3-methyl-2-cyclohexen-1-one, 1-acetyl-1-cyclohexene, 1-phenylsulfonyl-1,3-cyclohexadiene, 1,2-dichloroethene, diethyl ethylidenemalonate, 2-pentene, 4-methyl-5-vinylthiazole, butadiene sulfone, *trans*-cinnamonitrile, 4,4-dimethyl-2-cyclohexen-1-one, diphenyl alkyne, and vinyl ferrocene.

Conclusions

The use of tetraalkylammonium salts as electrolytes has been found to allow the formation of electrogenerated bases of especially high reactivity. Such conditions allow allyl phenyl sulfone to undergo addition, via its carbanion, to a variety of electron deficient vinyl and propenyl compounds (sulfone, ketone, nitrile, and ester). These Michael additions are catalyzed by electrogenerated bases derived from the reactant itself, rather than via an added pro-base. This work clearly displays the variety of substrates to which addition will occur, yet also highlights some important limitations in terms of yields. While several cases approach moderate 50% yields, the products formed from addition to sulfonyl compounds provide the most useful yields from this EGB approach. Where yields of "trimeric" 1:2 products exceed 90%, with addition occuring consecutively and selectively to 2 moles of vinyl sulfone. Mechanisms are advanced to explain the relative yields of dimeric and trimeric products, based upon the nature of the substrate molecule. The mechanisms for the formation of two secondary products from initial trimer products are also discussed. The formation of an eight membered thia ring from the α, γ position addition/cyclization of allyl phenyl sulfone carbanion to divinyl sulfone is unprecedented. Electrocatalytic factors for the majority of reactions are in excess of 10, representing better than 0.1 F mol^{-1} processes.

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CHAPTER VI

Further investigations of electrogenerated base chemistry

VI-1. Electrogenerated cyanomethyl anion addition reactions

The electrogenerated formation of cyanomethyl anions, and subsequent addition reactions, was first reported thirty years ago.[1] This initial work expanded to a number of of systems where electroreduction of aromatic carbonyl compounds lead to base formation, such that the substrates were themselves *in situ* "self-Pro-Bases" (self-PB), analogous to the allyl phenyl sulfone systems observed in chapter five. The difference comes in the lack of a readily removed proton from the substrate, such that the substrate PB deprotonates the acetonitrile solvent, giving an $-CH_2CN$ carbanion.[2] This reactive species is then seen to undergo nucleophilic attack upon the carbonyl group of the substrate.[3]

The reduction of two alkyl vinyl sulfones leads to effectively quantitative cyanomethylation, to give the corresponding cyano sulfones, with large catalytic factors of around 35. These products have been synthesized by non-electrochemical means, in multi-step processes, with just 30% yield of **15e**[4] and a better 87% yield of **15d**.[5]

Table VI-1. Yields of cyanomethylation of selected vinyl sulfones

Substrate	Extraction conditions	Yield of **15**	Catalytic factor
2e: Methyl vinyl sulfone	1:9 Water:Benzene	46	34
2e: Methyl vinyl sulfone	1:45 Brine:Benzene	92	31
2e: Methyl vinyl sulfone	1:23 Brine:Benzene	94	38
2d: Ethyl vinyl sulfone	1:23 Brine:Benzene	96	36
2b: Phenyl vinyl sulfone[a]	Dichloromethane +PTLC	31	4.9

[a]Not directly reduced, added to reduced diphenyl sulfone solution.

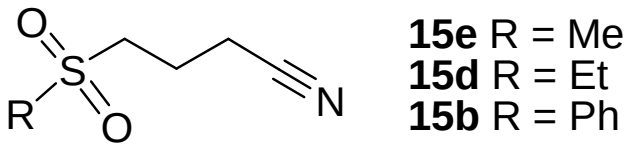


Figure VI-1. Cyanomethylation product, **15**, from the addition of EGB formed $-CH_2CN$ carbanion, to select vinyl sulfones.

The process for cyanomethylating phenyl vinyl sulfone (**9b**) was necessarily different, as reduction yields the cyclobutane dimer **2bb**. Initially a pro-base, diphenyl sulfone was co-reduced, yet this did not disrupt the anion radical cyclobutanation process. However, by reducing this pro-base in isolation, *ex situ* EGB generation, and then adding **9b**, appeared to give only **15b**. Separation gave a rather modest yield below the published value of 70%,[3] although that was via a multi-step "wet" synthesis. This pre-generation of base may well be a way to access a variety of cyanomethylation reactions, that would not normally get the opportunity to occur, due to a substrates given electroreactivity.

VI-2. Pro-base use in the improvement of allyl phenyl sulfone addition reactions.

The use of a pro-base, specifically diphenyl sulfone, has shown some initial promise in the yield improvement of allyl phenyl sulfone carbanion addition reactions, extensively discussed in chapter V. Those reactions proceed via formation of electrogenerated base from reduction of the ally phenyl sulfone itself, such that the substrate acts as a self-Pro-Base. While several of these reactions proceed extremely well (catalytically and in high yield), many addition reactions proceed to moderate yields of around 25% (albeit with reasonable catalytic rates). While initial attempts to improve yields have revolved around ratio and reduction time manipulation, promising results

have suggested that the use of an added pro-base could boost the addition product yield. Such an approach remains rather rare, an example being the use of *tert*-butyl alcohol as an added pro-base,[6] which was seen to boost the yield of an ester cyanomethlyation from 42% to 50% (30 mol%) and to 65% (100 mol%) in a stoichiometric arrangement. The use of diphenyl sulfone additive clearly allows for the formation of a greater amount of base during reduction, the key feature being that the base formed will necessarily be of similar strength to that formed from allyl phenyl sulfone reduction, as the basic anion radical is located upon the same moiety. It is apparent that in the case studied so far, such an increase in the appropriate strength base leads to a greater selection of the desired reaction pathway, improving yields. Indeed such an improvement in reaction efficiency/yield may well allow a reduction in the excess of substrate, over allyl phenyl sulfone, that is used.

The initial promising result is that of addition to phenyl acrylate, where a modest increase from a 22% to a 34% yield of the 1:1 product is observed, along with an increase in the catalytic factor, and even some recovery of unreacted substrate (around 13%). However, reaction with methyl acrylate suggests reduced promise for this approach, while 1:1 product and **9a** formation are effectively unchanged, and the catalytic factor is increased, both the 1:2 product (**11l**), and the cyclic **14l** that derives from **11l**, see depressed yields. It is worth taking into account the rather more complex nature of the methyl acrylate reaction, with its multitude of products. Such that an early increase of base may engender more side reactions (say polymerization, or even cyanomethylation), with the substrate. Indeed attempts to increase yields of the rather similar ethyl acrylate reaction (section V-9), by increasing substrate excess, were unsuccesful.

Table VI-2. Products and yields of attempted pro-base (diphenyl sulfone) enhanced allyl phenyl sulfone carbanion addition reactions.

Substrate[a]	% Yield of 1:1 product (**10**)	% Yield of 1:2 product (**11**)	% Yield of **9a**	% Yield of other products	Min. catalytic factor
Phenyl acrylate	22	-	24	-	1.5
Phenyl acrylate + 50 mol% diphenyl sulfone	34	-	18	-[b]	3.8
Methyl acrylate	16	18	8	**14l**: 12	2.5
Methyl acrylate + 50 mol% diphenyl sulfone	13	7	8	**14l**: 5	4.9

[a]Substrate present in apx. 2-fold excess, over **8**.
[b]Recovered 17mg of **9n**, no recovery in non-diphenyl sulfone reaction.

This area has yet to be extensively explored, especially to find the optimum amount of diphenyl sulfone additive. Ideally the amount of added pro-base should be kept low, due to the later need for separation, additionally, this should be feasible due to the catalytic nature of the reactions. Initial reactions have looked at 50 mole percent of the pro-base compared to allyl phenyl sulfone, although the intersection of cost/time-effectiveness, yield, and separation complications may well lay at a lower value.

There may prove to be an added complication, in that the pro-base may also lead to the deprotonation of propenyl substrates, as discussed below (VI-3), alongside enhanced allyl phenyl sulfone carbanion formation. This should not be too great a retarding factor as allyl compounds are generally more acidic than their propenyl counterparts (discussed below in VI-5), and substrate excesses could also be increased.

At this point it is rather unclear whether this approach will give significant yield increases for the allyl phenyl sulfone addition reactions. Preliminary assertions are being made on what are rather lower yields, and comparing values that are of similar

magnitude, such that differences may be effects of separation/workup. The phenyl acrylate result does withstand such scrutiny, with a reasonable yield increase (similar to those seen in the literature),[6] and evidence of improved efficiency in the use of substrate (recovered phenyl acrylate, not seen in the non-PB experiment). The question remains, in the first instance for addition to phenyl acrylate, whether increases in the mol% of diphenyl sulfone will increase yields yet further (again, as seen in the literature).[6]

VI-3. Pro-base use to form reactive non-allyl phenyl sulfone carbanions.

Diphenyl sulfone has also been employed as a pro-base to promote the formation of reactive carbanion species, via the deprotonation of either allyl or propenyl species. The true effectiveness of this approach remains to be seen, as the basicity of the reduced diphenyl sulfone (the EGB) may no longer be appropriate to the propenyl/allyl species under consideration. Several such species are already seen to undergo modest "self-EGB" based linear dimerizations, that a diphenyl sulfone pro-base may enhance. This may also be an area where EGB strength may be tuned via the use of different pro-bases, such as benzil and benzophenone (discussed in chapter II).[7]

Crotononitrile and phenyl propenyl ketone have been seen to form modest quantities of linear dimer, formed via their reduction in solution yielding an EGB that deprotonates another mole of substrate, with a subsequent addition entirely analogous to that seen for allyl phenyl sulfone self addition (product **10a**). Increases in the yield of these reactions, based on added diphenyl sulfone, have yet to be attempted.

An area of initial promise is that of methyl (and presumably ethyl) crotonate. While initial studies of cross-cyclobutanation with phenyl vinyl sulfone showed no cross

reaction (either anion radical or EGB promoted) it was thought that diphenyl sulfone could be employed to allow access to a reactive crotonate carbanion. So a 50 mol% addition to methyl crotonate, **9o**, and methyl acrylate, **9l**, (**9o**:**9l** = 1:2.18) reaction was attempted, with a degree of success as a modest 8% yield of the trimer **11oll** was obtained.

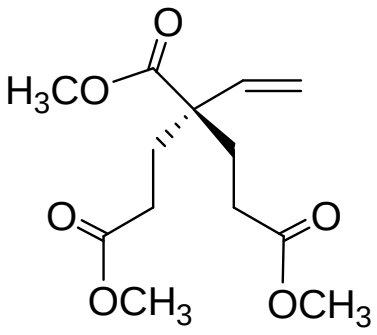


Figure VI-2. The trimeric product, **11oll**, formed from methyl crotonate, **9o**, carbanion addition to two moles of methyl acrylate, **9l**.

Amusingly, a similar ratio reaction minus the diphenyl sulfone appears to give an identical result (judged by NMR of the crude), which of course calls into doubt the utility of the pro-base in this case. It will however prove interesting to see if, with or without pro-base, the reactivity of the electrogenerated carbanion of alkyl crotonates can be exploited. For example, to give more of these trimeric products, say with other vinyl compounds such as the suite of compounds studied in chapter five.

Similar trimeric 1:2 addition products have been observed in minor quantities with phenyl and (particularly) biphe nyl propenyl ketone substrates, in cross reactions with phenyl vinyl sulfone. A number of electrolyses have been run with other substrates (instead of phenyl vinyl sulfone), both with and without pro -base, but have yet to indicate promise.

Interestingly, an attempted cross-cyclobutanation reaction between phenyl vinyl sulfone and 3-Penten-2-one, with added 20 mol% phenol, actually led to a reasonable 22% yield of the 1:2 trimeric product **11kbb**. The original idea of this experiment was to add a small amount of a weak acid, to suppress EGB mechanisms that might be faster than cyclobutanation. Phenol has been employed in electrolyses as a proton donor,[8] and used to trap EGB mechanism intermediates (section VI-4). However, phenol appears to be a relatively effective pro-base in this case. While broadly speaking electroreductive weak acids can act as pro-bases[9] I have not been able to locate specific use of phenol in this role. Indeed, an intriguing question comes to the fore, perhaps the phenol isn't acting as a pro-base, but rather as an anion radical cyclobutanation suppresent, as this reaction gives a miserly cyclobutane yield of 3%. The use of acetic acid[2] additive (stoichiometrically) actually stops all reactions, corroborating this idea, as the acid is now strong enough (and at sufficient concentration) to stop not only anion radical pathways, but also EGB pathways. The addition of diphenyl sulfone at 30mol% does not appear to affect the normal cross-cyclobutanation reaction, in fact no EGB trimeric product is seen in this case. Perhaps more added pro-base will allow exclusive access to **11kbb**.

VI-4. Addition of acid to electrogenerated base reactions, intermediate trapping.

Initial work in this area has revolved around the use of different strength added acids that will interupt the self addition of allyl phenyl sulfone, **8**, under reductive electrolysis. A handful of select acids have been used, allowing a range of reaction interuptions to be observed, from complete supression of carbanion formation (as evidenced by the lack of propenyl phenyl sulfone, **9a**, formation) through mixtures of **8** and **9a** (acid trapping of the carbanion) without any formation of **10a**.

Table VI-3. Summary of attempts to trap EGB intermediates with acid additives

Acid (Substrate)	**8**:Acid:Substrate	%charge used	Result
Malononitrile	1:1.00	50	No reaction
Phenol	1:0.51	100	No coupling (formation of **10a**), formed **9a**, 3.41:1 excess over **8**
D_2O	1:50	35	No coupling (formation of **10a**), formed **9a**, 2.89:1 excess over **8**
H_2O	1:30	100	No **9a** or **8**, 14% **10a**, 19% **16a**, 11% methyl phenyl sulfone
Acetic acid Phenyl vinyl sulfone (**9b**)	1:1.10:2.17	83	No reaction
Phenol Phenyl vinyl sulfone (**9b**)	1:1.06:2.15	100	No coupling (formation of **10a**), formed **9a**, 3.82:1 excess over **8**, also some **2bb**.
Ethanol Phenyl vinyl sulfone (**9b**)	1:1.12:2.13	8	Just **11b**
D_2O Phenyl vinyl sulfone (**9b**)	1:5.41:2.09	7	Just **11b**

Malononitrile, a common electrochemical proton donor,[10] appears to be too strong an acid, in that it prevents all EGB activity, even with relatively extended reduction time (using 50% of charge). Phenol and D_2O appear to be of more appropriate strength, in that they prevent coupling of the carbanion to the *in situ* formed propenyl **9a**.

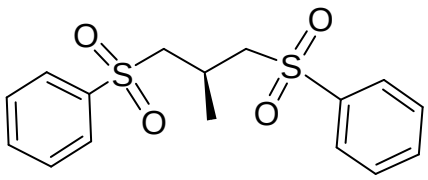
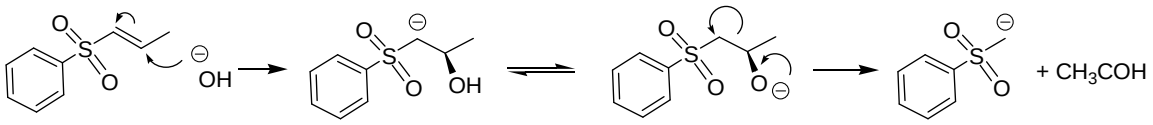


Figure VI-3. The product, **16a**, of *in situ* formed methyl phenyl sulfone carbanion addition

The use of water appears to allow some coupling to form **10a**, along with additional coupling of an *in situ* formed carbanion, of methyl phenyl sulfone.[11] This leads to a modest yield of **16a**, which is shown in figure VI-2, from this carbanion coupling to, presumably, the β position of **9b (**rather than to **8**). A postulated reaction scheme is given in scheme VI-1, which is supported by the recovery of methyl phenyl sulfone. Although it is interesting to note that experiments with methyl phenyl sulfone show that it does not readily deprotonate during reduction, either when present with **8** (1:1 ratio), or with **8** and diphenyl sulfone (1:1:1 ratio).



Scheme VI-1. How the presence of water could lead to the formation of a reactive methyl phenyl sulfone carbanion.

VI-5. Isomerization via electrogenerated bases

The effect of added weak acids, such as phenol, to a reductive electrolysis of allyl phenyl sulfone, is to allow an isomerization to occur, from allyl to propenyl. However, in circumstances where an allyl substrate can be reduced to form an EGB, yet there is no competition with self addition, for example, due to a stearic interference, then EGB formation may allow for an electrocatalytic isomerization pathway. Clearly this set of circumstances only applies to a select group of compounds, indeed as yet this has only been observed with allyl phenyl sulfide, and allyl phenyl sulfone with acid additives.

It is interesting to note the allyl to propenyl ratio, which equates to around 75% conversion to propenyl, a value that is seen for a series of phenol (and D_2O, in table VII-2) reactions. This may well represent a thermodymanic equilibria between the two isomers, as even extended reduction does not force the isomerization to just the propenyl form. Using around a third of the required charge is sufficient to achieve this ratio, as is 50 mol% of phenol. Reducing the amount of phenol below this, to 30 mol%, leads to some formation of the addition product, **10a**.

Table VI-4. Summary of attempts to use acid additives to isomerize allyl phenyl sulfone (**8**) to propenyl phenyl sulfone (**9a**) .

8:Phenol	%charge used	Result
1:0.51	100	No coupling (formation of **10a**), formed **9a**, 3.41:1 excess over **8**
1:0.50	36	No formation of **10a**, formed **9a**, 3.20:1 excess over **8** additional minor amount (6%) of unknown coupling product (see experimental)
1:0.30	100	Formed **10a**, and **9a** (1:1.94), Small amount of unreacted **8**

An additional approach to isomerizing allyl phenyl sulfone, is to pre-generate the EGB, and then add **8**. The intention here would be to limit the amount of base available, so possibly prevent the reaction going to completion and giving **10a**. Clearly this is a catalytic reaction, so the exact amount of EGB to be created, by pro-base reduction, may well be difficult to judge. This has been attempted with a stoichiometric amount of diphenyl sulfone for 12% of required charge, the addition of **8** lead to the regular, non-pregeneration, high yield formation of **10a** (with trace **9a**). A second attempt, with 34 mol% benzil, appears more promising, with a suppresion of **10a** formation, and 2.54:1

ratio of **9a**:**8**, using just 11% of required charge. While several of these reactions are on the 200 mg scale, with unreacted **8** present it has proven rather difficult to separate out the desired propenyl isomer, **9a**, using PTLC methods.

Isomerization of allyl phenyl sulfide has yielded some success, with a 33% recovered yield of the propenyl isomer. Although more than 80% of the required charge was used, this may yet prove excessive. Indications from the crude NMR suggest the reaction may well be quantitative, as no allyl isomer was observed. Further reactions to assess the reactivity of the necessarily formed carbanion intermediate have yet to yield positive results. Both via co-reduction with **8**, which leads to **10a** and no isomerization (small amount of charge used), and initial reduction of allyl phenyl sulfide in isolation (for 50% of required charge) followed by addition of **8** (and 2.0 C of additional charge), lead to complete isomerization (from NMR of crude extract), along with **10a**, but no cross-coupling (checked by LRMS).

Isomerization of allyl phenyl ether has proven unsuccessful, both by electroreduction in isolation, and with 50 mol% diphenyl sulfone additive. Indeed, it seems likely that a carbanion is not being formed, electrolysis alongside an excess of phenyl vinyl sulfone yields no cross-reaction (although **2bb** is readily formed).

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CONCLUSION

This thesis has displayed the utility of a number of electrochemical synthetic routes. The intramolecular pericylcic reactivity of a wide range of bis(enones) has been studied, such that a clear picture of the mechanism and scope have emerged. The use of alkylammonium salts as electrolytes in acetonitrile solutions, has been found to afford the most promising synthetic approach. A system that has been applied to intermolecular cyclobutanation, affording just the third class of examples of this anion radical promoted cycloaddition. The use of metal perchlorate salts appears less attractive in terms of absolute yield, but does display interesting stereoselectivity possibilities.

A variety of electrogenerated themes have been addressed. While these mechanisms are viewed as yield reducing side reactions in the anion radical work, their utility elsewhere is manifest. The self pro-basic nature of allyl phenyl sulfone, and the subsequent reactive carbanion, have been extensively probed. These reactions are characterized by high rates of catalysis, and in many cases, by excellent yields. The continuing diversification of electrogenerated base chemistry has also been glimpsed.

While the limitations to electroorganic synthesis are clear, it can provide an attractive high yield and importantly “green” approach to entirely novel compounds. In many cases the only reactant is the charge flowing through the system, which is seen throughout this work to lead to catalytic processes.

FUTURE DIRECTIONS

The number of electrogenerated base threads discussed in chapter six are clear indications of future directions. Firstly, the scale up of cyanomethylation reactions, and indeed application of the pro-base EGB pre-generation method to other compounds, particularly those that are usually electroreductive. Secondly, the formation of more 1:2 trimeric products, again via a pro-base, this time to give carbanion to substrate additions analogous to those seen for allyl phenyl sulfone. Lastly, using pro-base to help improve the yield of allyl phenyl sulfone carbanion addition reactions, although this may prove a tougher target, as shown by initial experiments.

The anion radical cyclization work can also be further expanded. Possibly by the use of substituted propenyl/vinyl ketones, again in cross reactions with phenyl vinyl sulfone. It would interesting to attempt intramolecular cyclization work in, for example, total molecule synthesis.[1] This could allow observation of how sensitive other functional moieties are under electroreductive conditions. Even whether fine electrochemical control could help select for anion radical cyclization alone. The rather dramatic diastereoselective effect of varied metal perchlorate electrolytes could also provide an interesting starting point for further research. For example, could a known non-electrochemical reaction be run in tandem with a slight electrical current,[2] so as to set up an ion-pair in the solution. The subsequent reacting moiety may then be directed to a preferential diastereomer.[3] This may be a reach, but such a scheme should be at least be applicable to some published electrochemical cyclizations (usually electrohydrocyclizations).[4]

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EXPERIMENTAL

ANALYSIS

Room temperature ^{1}H NMR spectra were recorded on a Varian Unity+ 300 as solutions in $CDCl_3$. ^{13}C NMR and COSY spectra were recorded on a Varian Unity Inova 500 spectrometer. Chemical shifts (δ) are relative to tetramethylsilane, and coupling constants (J) are given in Hertz (Hz). Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublets; br, broad. X-ray diffraction analyses were conducted using a Nonius Kappa CCD diffractometer. Crystallographic data (excluding structure factors) has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC# where noted. Copies of the data can be obtained, free of charge, via *www.ccdc.cam.ac.uk /data_request/cif* or on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk). Low-resolution mass spectra (LRMS) were recorded on a Finnigan MAT TSQ-70 mass spectrometer, with high-resolution mass spectra (HRMS) recorded on a VGZAB-2E mass spectrometer.

GENERAL PROCEDURE

A typical experiment utilizes 80-100 mg of substrate, along with the described mole ratio, if appropriate, of additional reactants. In general, all substrates are dissolved in 22 mL of electrolyte solution, giving a typical substrate concentration of 0.025 M, or 0.0150 M for bis(enone) experiments. This electrolyte/substrate solution is added to the working electrode (WE) compartment of the electrolysis cell. The electrolyte is generally

in dry acetonitrile, and is either 0.100 M Et_4NBF_4, or 0.100 M perchlorate salt (unless stated). The acetonitrile is distilled fresh for each electrolysis from a reservoir containing phosphorus pentoxide. On occasion that THF is used, it is freshly distilled from a blue solution of sodium and benzophenone. Electrolyte solution (6 mL) is added to the counter electrode (CE) compartment. The solution is stirred, via a stir bar in the WE compartment, for ten minutes before initiating electrolysis.

Electrolysis was carried out at controlled potentials stated later, in each case with stirring under positive nitrogen flow at room temperature. Electrolysis potentials were versus a "pseudo-standard" silver wire (encased in porous vycor glass) reference electrode (RE).[1] The RE used is seen to have a calibration to SCE of approximately +0.1 V, when in 0.1 M Et_4NBF_4 acetonitrile solution. The RE when measured against Cl^- | AgCl | Cl reference electrode using 1.0 M KCl electrolyte gave a potential of +0.090 V. The RE was placed in a 0.1 M Et_4NBF_4 acetonitrile solution, connected via a saturated KCl salt bridge. Using the known E^0 for the Ag/AgCl reference (+0.237 V vs. SHE)[2] we get a calibration of +0.327 V for our reference electrode vs. SHE, equivalent to +0.085 V vs. SCE. Given the inherent error involved it is most reasonable to quote a calibration as +0.1 V vs. SCE. This means that an electrolysis at -1.5 V vs. RE equates to an electrolysis at -1.4 V vs. SCE.

The CE and WE consisted of reticulated vitreous carbon (25 mm x 5 mm x 5 mm), their corresponding compartments separated by a course frit. The RE was placed within 0.5 cm of the WE. The reaction was stopped when thin-layer chromatography (TLC) indicated that the limiting substrate had been consumed. The reactant solution (WE compartment only) then underwent an aqueous workup with sequential washings of

dichloromethane (benzene when noted). The organic phase was retained and dried with Na_2SO_4. The dichloromethane was removed by rotary evaporation, with the crude solution being purified by preparative TLC (1 mm thick, elution with ethyl acetate/petroleum ether mixture, 1:1.5 to 1:9 ratios). Bands were identified, collected by scraping, and extracted with dichloromethane. Filtering removed the silica, with a rotary evaporator again employed to remove the solvent, yielding the desired products.

EQUIPMENT/REAGENTS

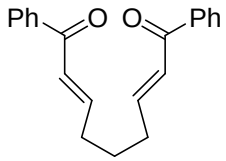
A potentiostatic controller, the Electrosynthesis Company (ESC) model 415, was used to control the applied potential. The charge used was tracked by a digital coulometer, ESC model 640. The applied potential was confirmed using a digital multimeter (Wavetek DM7), operating as a potentiometer. The electrode material was Duocel 80 PPI reticulated vitreous carbon. The bis(enone) substrates were kindly produced within the Krische[3] group or by Dr. Jingkui Yang,[4] both at the University of Texas at Austin. Dr. Jingkui Yang was also responsible for the synthesis of phenyl propenyl ketone and biphenyl propenyl ketone. Reagent purity was assayed by NMR/LRMS. All other substrates and electrolytes were used as purchased, from Alfa Aesar, Aldrich, and Lancaster (98-99% purity, except for 3-Penten-2-one: 85 and 90%, which is corrected for in ratio calculations). ACS grade benzene and dichloromethane used in work up, were used as purchased from Fisher. TLC plates and PTLC plates were used as purchased from Sorbent Technologies (250 μm and 1 mm thick, glass backed, Silica G-Prep, uv254 indicator)

All glassware was oven-dried prior to use, with the electrolysis cell being stored in a sodium hydroxide/2-propanol base bath between experiments. The cell was periodically cleaned with a potassium dichromate/sulfuric acid solution. The weighed electrolyte was place under vacuum for ~30 mins prior to dissolution in solvent, as were many substrates (exceptions were for volatile limiting reagents, and are noted below). On occasion Tetrahydrofuran (THF) was used as the electrolyte solution, in such cases it was distilled from a blue solution of sodium and benzophenone.

An undivided cell was used for two reactions, using apx. 50% of the required charge. Phenyl vinyl sulfone reduced in this manner gave minor amounts of an unknown product, but primarily unreacted phenyl vinyl sulfone. Methyl vinyl sulfone displayed no reaction, simply returning unreacted starting substrate. These results clearly support the use of a divided cell, for the reactions studied.

CHAPTER II

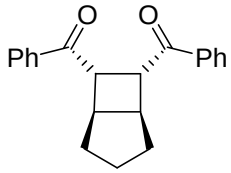
The electrolysis of a variety of bis(enones) was carried out per the above general electrolysis procedure, with specific conditions detailed below. Early reactions were run with Bu_4NBF_4 electrolyte, however the non-aqueous solution solubility of this compound led to occasional separation problems, particularly given the scale of much of this work. Hence, a change was made to Et_4NBF_4 electrolyte, with no apparent change in reactivity, but greatly improved ease of separation of crude mixtures. In cases when starting material is recovered, the yields of products and the catalytic factors are corrected accordingly. Characterization of products was in most cases completed by comparison to the products obtained from **1b** electrolysis, the products from **1b** are therefore more fully characterized both by 500 MHz NMR ($^1H/^{13}C$) and HRMS. Their ready crystallization also allowed for x-ray structural determination . All novel products are also characterized by HRMS or, in two further cases, by x-ray crystallography. CCDC numbers quoted where deposited. A handful of previously observed compounds are only characterized by NMR and referenced appropriately.



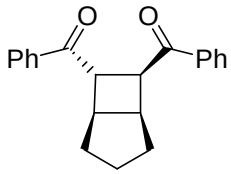
Electrolysis of E,E -1,7-dibenzoyl-1,6-heptadiene (1a)

Electrolysis of 111 mg (0.0166M) of **1a** with 0.100 M Bu_4NBF_4 electrolyte, at -2.0 V vs. RE (first 3.0 C at -1.5 V). The reaction appeared complete after 7.5 C, o r 21.3% (of required charge) had passed through the cell. PTLC purification of the 105 mg of recovered crude yielded *cis*-**2a** (19 mg, 17%), *trans*-**2a** (65 mg, 59%), and **3a** (14 mg,

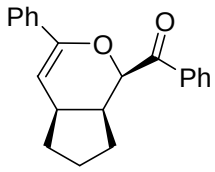
13%) for a total of 98 mg of pericyclic products (88%). No starting material was recovered, and no other products were identified.



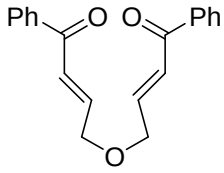
cis-**2a**[3]**:** ^{1}H NMR (300 MHz, $CDCl_3$): 1.65 (2H, m), 1.84 (2H, m), 2.02 (2H, m), 3.20 (2H, br.s), 3.85 (2H, d 4.2 Hz), 7.35 (4H, br.t 7.2 Hz,), 7.44 (2H, br.t 7.2 Hz), 7.75 (2H, br.d 8.1 Hz).



Trans-**2a**[3]: ^{1}H NMR (300 MHz, $CDCl_3$): 1.42 (2H, m), 1.52 (1H, m), 1.85 (3H, br.m), 3.06 (1H, q 6.9 Hz), 3.24 (1H, m), 4.28 (1H, dd 6.6, 7.5 Hz), 4.57 (1H, dd 7.8, 10.5 Hz), 7.46 (4H, m), 7.55 (2H, m), 7.95 (2H, br.d 6.9 Hz), 8.02 (2H, br.d 7.2 Hz).



3a[3]: ^{1}H NMR (300 MHz, $CDCl_3$): 1.60 (2H, m), 1.84 (2H, m), 2.01 (2H, m), 2.69 (2H, m), 4.89 (1H, d 6.6 Hz), 5.59 (1H, d 3.0 Hz), 7.26 (3H, m), 7.48 (4H, m), 8.08 (2H, d 7.5 Hz).



Electrolysis of E,E -1,7-dibenzoyl-4-oxa-1,6-heptadiene (1b)

Electrolysis of 100 mg (0.0149M) of **1b** with $Mg(ClO_4)_2$ electrolyte, at increasing voltages vs. RE. The first 3.0 C at -2.0 V, then 1.8 C at -3.0 V, followed by 1.3 C at -3.5 V, and 6.0 C at -4.0 V. The reaction appeared complete after 12.1 C, or 38.4% (of the

required charge) had passed through the cell. PTLC purification (1:4 ratio of EA:PET) of the 156 mg of recovered crude yielded *cis*-**2b** (26 mg, 39%), *trans*-**2b** (14 mg, 21%), and **3b** (19 mg, 28%), giving a total of 59 mg of pericyclic products (88%). While no other products were identified, 33 mg of starting material was recovered. The above percent of required charge is based upon the 100 mg of starting material being used up; this becomes 54.8% based upon the 67 mg of starting material used up (not recovered).

Electrolysis of 205 mg (0.0305M) of **1b** with $LiClO_4$ electrolyte, at -1.3 V for 40.0 C (62.7% of required charge). PTLC separation of the 170 mg of crude yielded *cis*-**2b** (41 mg, 20%), *trans*-**2b** (42.2 mg, 21%), **3b** (4 mg, 2%), along with 2.8 mg of unreacted **1b**.

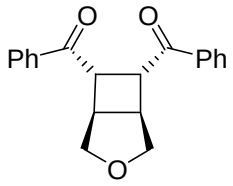
Electrolysis of 105 mg (0.0156M) of **1b** with Bu_4NBF_4 electrolyte, at -1.6 V for 2.1 C and -2.0 V for 0.9 C. This corresponds to 9.4% of required charge. PTLC separation of the 108 mg of crude yielded *cis*-**2b** (12 mg, 11%), *trans*-**2b** (41 mg, 39%), **3b** (3 mg, 3%), and **4b** (11mg, 11%).

Electrolysis of 28 mg (0.0042M) of **1b** with Et_4NBF_4 electrolyte, and 157 mg (0.340M) of benzil, at -1.4 V for 3.2 C. This corresponds to 36.2% of required charge, or a catalytic factor of 2.76. PTLC separation proved problematic due to the large benzil excess, however a yield of 19.1 mg (68%) of **4b** was obtained by NMR integration of several mixed **4b**/benzil PTLC bands. No other products or unreacted starting material were observed.

Electrolysis of 66 mg (0.0098M) of *cis*-**2b** with $LiClO_4$ electrolyte, at -2.5 V for 27.5 C, -3.0 V for 4.5 C, and then at -3.5 V for a further 30.0 C. PTLC separation of the crude yielded *trans*-**2b** (17.3 mg, 32%), **3b** (4 mg, 7%), an aldol product **6b** (5.7 mg,

11%), a dihydro product **7b** (11 mg, 20%), with a further 12 mg (18%) of unreacted *cis*-**2b.**

Electrolysis of 52 mg (0.0077M) of *trans*-**2b** with $LiClO_4$ electrolyte, at -3.0 V for 11 C, -3.5 V for 130 C, and – 4.0 V for 20 C. No product spots were observed until after ~40 C, indicating that no reaction was occurring, hence the continued flow of charge. PTLC of the 68 mg of crude yielded 8 mg of impure *trans*-**2b**, along with 19mg of unidentified product (single benzoyl moiety). None of the characterized products (such as *cis*-**2b**) were observed.



Cis-**2b**: ^{1}H NMR (500 MHz, $CDCl_3$): 3.42 (2H, m), 3.63 (2H, d.m 10.2 Hz), 4.14 (4H, m), 7.34 (4H, br.t 7.6 Hz), 7.45 (2H, br.t 7.3 Hz), 7.72 (4H, br.d 8.2 Hz); ^{13}C NMR (500MHz in $CDCl_3$): 39.72, 47.70, 73.46, 127.81, 128.59, 132.8, 136.05, 198.08; NMR COSY (500 MHz), and X-ray crystallography confirm structure; HRMS (CI+): Calc; 307.133420, Found; 307.132575.

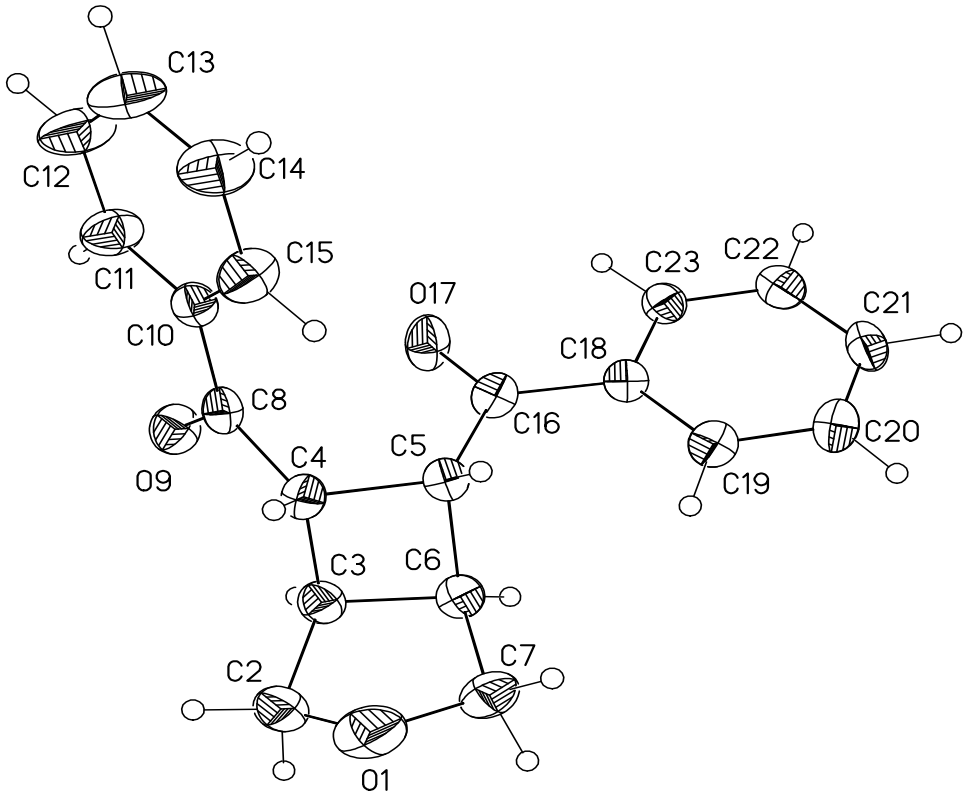
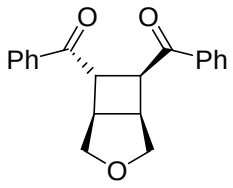


Figure E-1: View of *Cis*-**2b** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.



Trans-**2b**: ^{1}H NMR (500 MHz, $CDCl_3$): 3.36 (3H, br.m), 3.46 (1H, dd 4.6 Hz, 9.6 Hz), 3.68 (1H, d 9.8 Hz), 4.06 (1H, d 9.6 Hz), 4.41(1H, m), 4.53 (1H, m), 7.45(4H, m), 7.54 (2H, br.m), 7.90 (2H, m), and 8.01 (2H, m); ^{13}C NMR (500 MHz in $CDCl_3$): 39.71, 40.74, 42.99, 43.01, 69.27, 72.55, 128.29, 128.71, 128.76, 128.91, 133.41, 133.43, 135.27, 135.61, 196.70, 199.70; NMR COSY (500 MHz), and X-ray

crystallography confirms the structure; HRMS (CI+): Calc; 307.133420, Found; 307.133048.

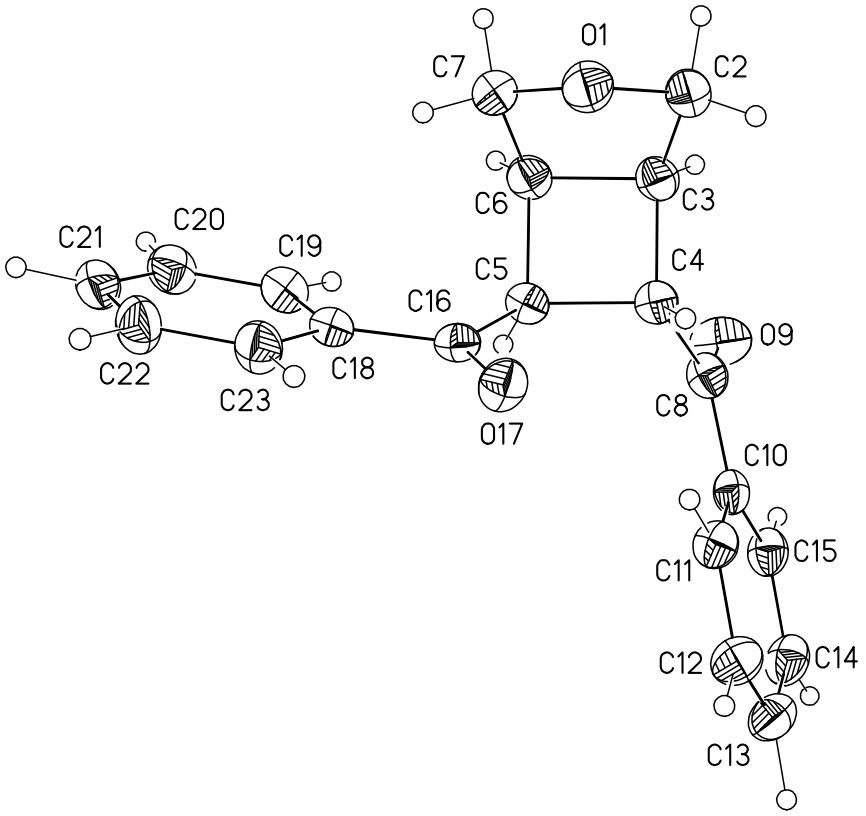
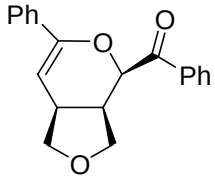


Figure E-2: View of *Trans*-**2b** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.



3b: ^{1}H NMR (500 MHz, $CDCl_3$): 2.99(1H, m), 3.06 (1H, m), 3.58 (1H, m), 3.75 (1H, dd 4.4 Hz, 9.6 Hz), 4.17 (2H, m), 4.98 (1H, d 8.6 Hz), 5.58(1H, d 4.2 Hz), 7.26(2H, m), 7.48 (5H, m), 7.61 (1H, m), 8.08 (2H, m); ^{13}C NMR (500MHz in $CDCl_3$):

35.54, 36.94, 70.30, 74.03, 76.30, 98.89, 124.65, 128.24, 128.44, 128.62, 129.51, 133.70, 134.44, 135.41, 151.80, 196.01; NMR COSY (500 MHz) and X-ray crystallography confirms the structure; HRMS (CI+): Calc; 307.133420, Found; 307.132957.

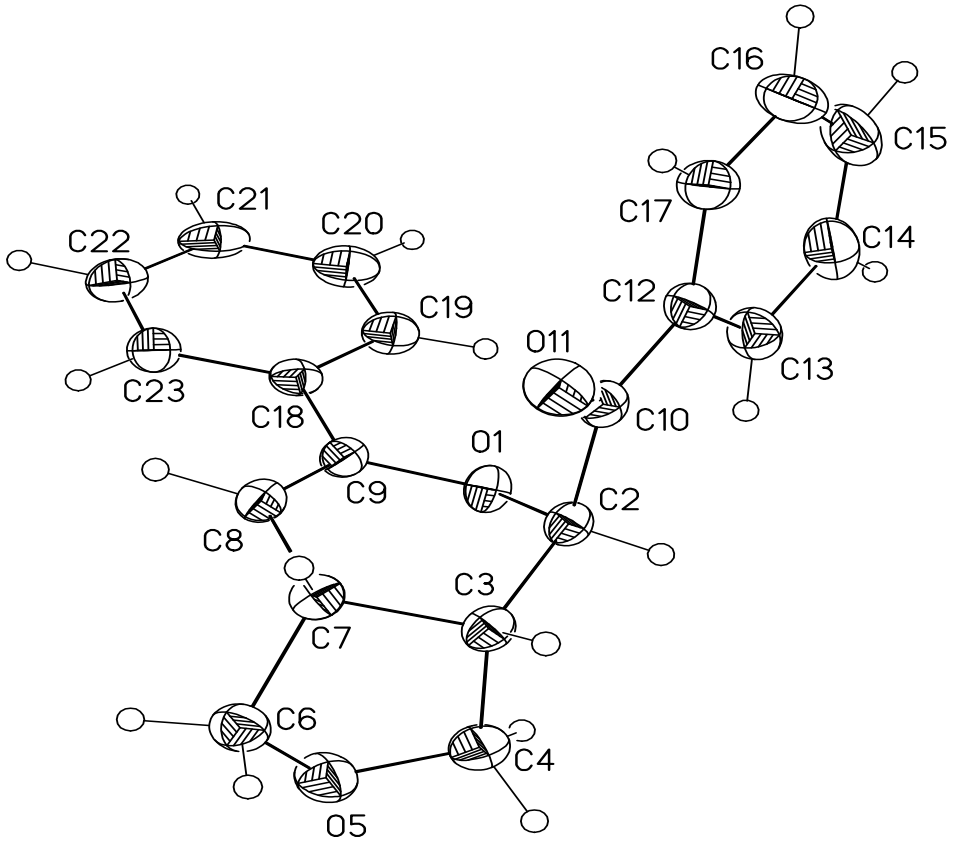
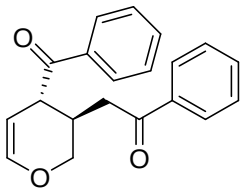


Figure E-3: View of **3b** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.



4b: ^{1}H NMR (300 MHz, $CDCl_3$): 3.08 (1H, m), 3.17 (1H, d 5.7 Hz), 3.20 (1H, d 7.5 Hz), 3.85 (1H, m), 3.98 (1H, dd 3.3, 10.8 Hz), 4.23 (1H, dd 2.7, 10.8 Hz),

4.72 (1H, td <1.5, 6.0 Hz), 6.52 (1H, dd 1.8, 6.0 Hz), 7.48 (4H, br.t 7.5 Hz), 7.58 (2H, m), 8.00 (4H, m). X-ray crystallography confirms structure (CCDC 240331)

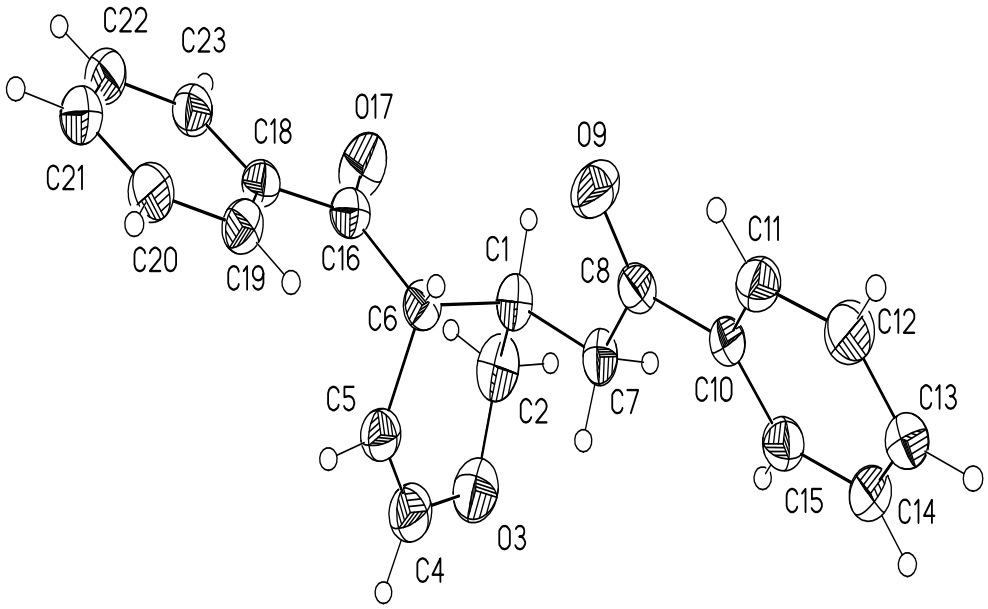
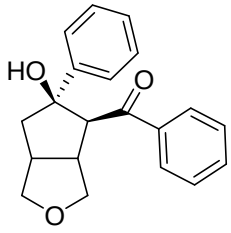


Figure E-4: View of **4b** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. CCDC 240331.



6b: ^{1}H NMR (300 MHz, $CDCl_3$): 1.98 (1H, ddd 1.5, 8.1, 12.9 Hz), 2.45 (1H, dd 8.1, 12.9 Hz), 3.22 (2H, m), 3.64 (2H, dd 6.3, 9.0), 3.85 (2H, t 9.9 Hz), 4.12 (1H, d 9.6 Hz), 5.35 (1H, d 2.1 Hz), 7.14 (1H, m), 7.24 (2H, m), 7.40 (2H, m), 7.52 (2H, m), 7.59 (1H, m), 7.80 (2H, dd 1.5, 8.7 Hz). X-ray crystallography confirms the structure.

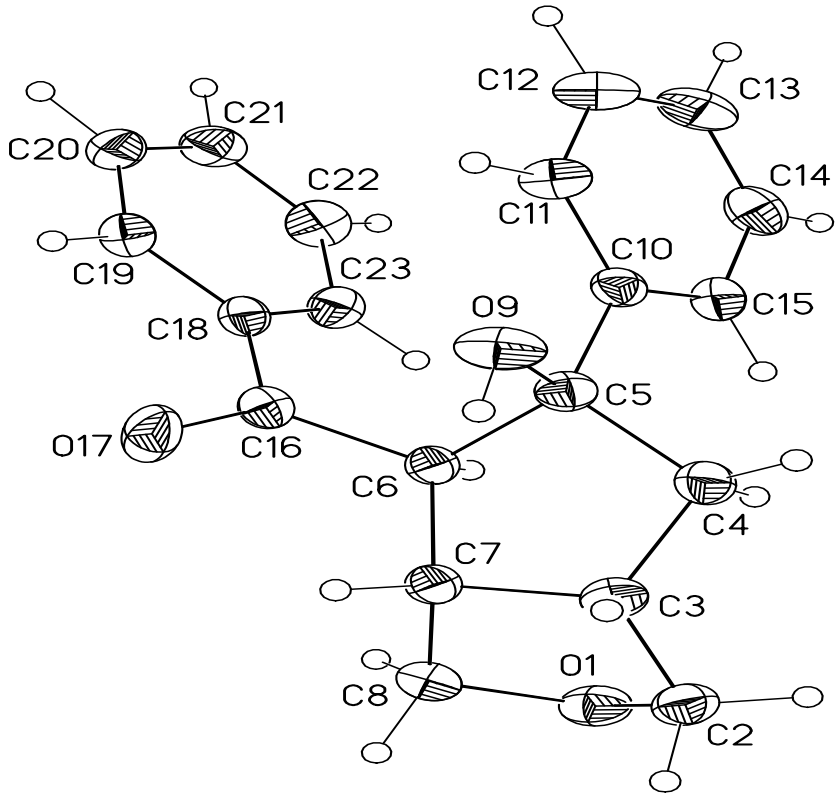
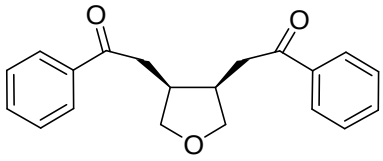
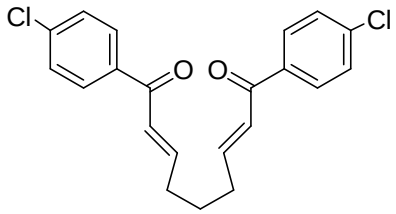


Figure E-5: View of **6b** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.



Cis-**7b**: ^{1}H NMR (300 MHz, $CDCl_3$): 3.04 (4H, br.m), 3.16 (2H, dd 3.0, 14.1 Hz), 3.60 (2H, dd 4.2, 8.7 Hz), 4.12 (2H, m), 7.47 (4H, br.t 7.8 Hz), 7.58 (2H, br.t 7.8 Hz), 7.94 (4H, m); HRMS (CI+): Calc; 309.149070, Found; 309.149110.

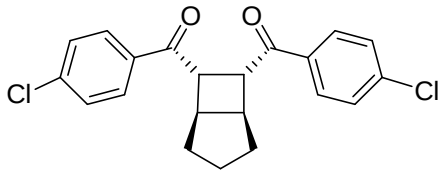


Electrolysis of E,E-1,7-bis(4-chlorobenzoyl)-1,6-heptadiene (1c)

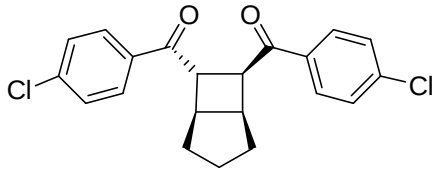
Electrolysis of 99 mg (0.012 M) of **1c** with Bu_4NBF_4 electrolyte, at -1.2 V for 2.1 C, -1.6 V for 2.2 C, and -1.8 V for 0.8 C. The reaction appeared complete after 5.0 C, or 19.5 % (of required charge) had passed through the cell. PTLC purification of the 124 mg of recovered crude yielded *cis*-**2c** (11 mg, 11%), *trans*-**2c** (51.5 mg, 52%), and **3c** (11.5 mg, 12%), for a total yield of 74 mg of pericyclic products (75%). No starting material was recovered. However, a further 5 mg (5%) of **5c** was recovered.

Electrolysis of 55 mg (0.0067 M) of **1c** with 32 mg (0.0080M) of benzophenone and Et_4NBF_4 electrolyte, at -1.8 V for 1.5 C (10.5% of required charge). **1c**:benzophenone = 1:1.19. PTLC separation yielded *cis*-**2c** (6 mg, 11%), *trans*-**2c** (23 mg, 42%), and **3c** (4 mg, 7%), for a total yield of 33 mg of pericyclic products (60%). A further 7 mg (13%) of **5c** was recovered.

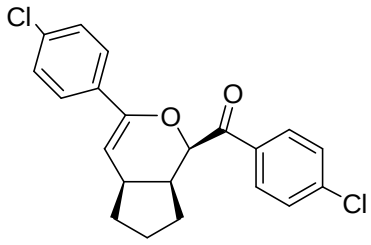
Electrolysis of 99 mg (0.012 M) of **1c** with 165 mg (0.036 M) of Benzil and Et_4NBF_4 electrolyte, at -1.3 V for 2.5 C (9.7% of required charge). **1c**:benzil = 1:1.2.96. PTLC separation yielded 28 mg (28%) of **5c** along with 42 mg (42%) of an unidentified polymer.



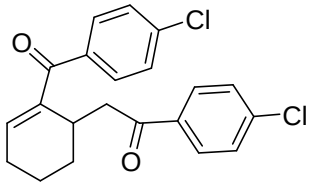
cis-**2c**: ^{1}H NMR (300 MHz, $CDCl_3$). 1.68 (2H, m), 1.82 (2H, dd 9.9,2.4 Hz), 2.00 (2H, m), 3.16 (2H, m), 3.77 (2H, d 3.9 Hz), 7.32 (4H, d 8.4 Hz), 7.66 (4H, d 9.0 Hz); HRMS (CI+): Calc; 373.076210; Found 373.076164.



trans-**2c**: ^{1}H NMR (300 MHz, $CDCl_3$): 1.38 (2H, m), 1.58 (1H, m), 1.82 (3H, m), 3. 04 (1H, dd 6.9, 13.2 Hz), 3.22 (1H, m), 4.20 (1H, dd 0.9 Hz, 7.5 Hz), 4.49 (1H, dd 2.4, 10.2 Hz), 7.44 (4H, dd 2.7, 8.4 Hz), 7.88 (2H, br. d 8.4Hz), 7.95 (2H, br.d 9.0 Hz):); HRMS (CI+): Calc; 373.076210, Found; 373.075821.

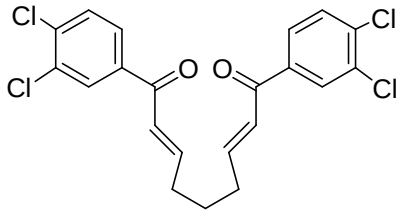


3c: ^{1}H NMR (300 MHz, $CDCl_3$): 1.41 (1H, m), 1.59 (2H, m), 1.78 (1H, m), 2.01 (2H, m), 2.68 (2H, m), 4.80 (1H, d 6.9Hz), 5.52 (1H, d <1.5 Hz), 7.40 (2H, m), 7.47 (4H, m), 8.01 (2H, d 8.4 Hz); HRMS (CI+): Calc; 373.076210, Found; 373.076898.



5c: ^{1}H NMR (300 MHz, $CDCl_3$): 1.64 (1H, m), 1.72 (3H, m), 2.30 (2H, br.m), 2.79 (1H, dd 10.2, 14.7 Hz), 3.34 (1H, dd 3.6, 14.7 Hz), 3.43 (1H, br.s),

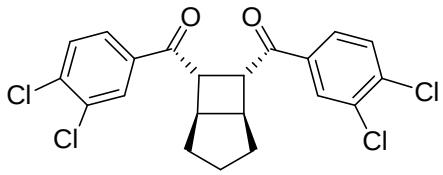
6.61 (1H, td 3.9, 1.2 Hz), 7.43 (3H, m), 7.51 (1H, m), 7.62 (2H, m), 7.99 (2H, m); HRMS (CI+): Calc; 373.076210, Found; 373.076307.



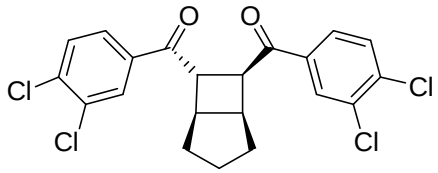
Electrolysis of E,E-1,7-bis(3,4-dichlorobenzoyl)-1,6-heptadiene (1d)

Electrolysis of 102 mg (0.0105 M) of **1d** with $LiClO_4$ and $Mg(ClO_4)_2$ electrolyte (both 0.10 M), at -4.0 V (first 1.5 C at -3.0 V). The reaction appeared complete after 17.0 C, or 76.3% (of required charge) had passed through the cell. PTLC purification of the 87 mg of recovered crude yielded *cis*-**2d** (34 mg, 33%), *trans*-**2d** (7 mg, 7%), and **3d** (16 mg, 16%), for a total yield of 57 mg of pericyclic products (56%). A further 6 mg (6%) of a product was isolated and identified as **6d**.

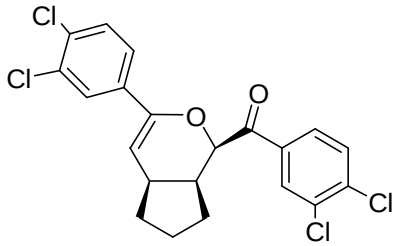
Electrolysis of 100 mg (0.0103 M) of **1d** with Et_4NBF_4 electrolyte, at -3.2 V for 3.0 C (first 0.75 C at- 2.5 v, then 0.75 C at -3.0 V). This corresponds to 13.7% of required charge. PTLC purification of the 150 mg of crude yielded 3 mg (3%) of *trans*-**2d**, 17 mg (17%) of **5d**, and 35 mg (35%) of an unidentified polymer.



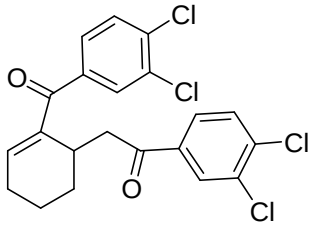
cis-**2d**: ^{1}H NMR (300 MHz, $CDCl_3$): 1.74 (2H, m), 1.85 (2H, dd 11.7,3.3 Hz), 2.05 (2H, m), 3.19 (2H, d 2.4 Hz), 3.77 (2H, d 3.6 Hz), 7.46 (2H, d 8.4 Hz), 7.57 (2H, dd 8.7, 2.1 Hz), 7.81 (2H, d 2.1 Hz); HRMS (CI+): Calc; 440.998266; Found; 440.997859.



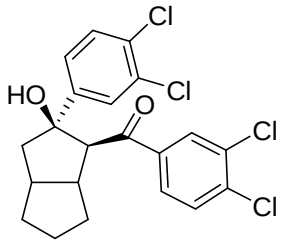
trans-**2d**: ^{1}H NMR (300 MHz, $CDCl_3$): 1.38 (2H, m), 1.55 (1H, m), 1.83 (3H, m), 3.04 (1H, m), 3.24 (1H, m), 4.15 (1H, m), 4.47 (1H, dd 2.1 Hz, 10.2 Hz), 7.55 (1H, d 3.3 Hz), 7.57 (1H, d 3.0 Hz), 7.76 (1H, br.d), 7.81 (1H, br.d), 8.02 (1H, d 2.1 Hz) 8.08 (1H, d 1.8 Hz); HRMS (CI+): Calc; 440.998266, Found; 440.997697.



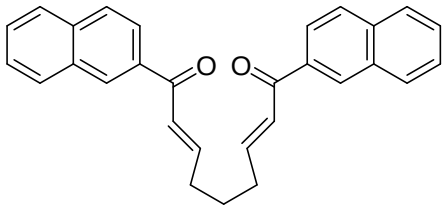
3d: ^{1}H NMR (300 MHz, $CDCl_3$): 1.60 (2H, m), 1.85 (2H, m), 2.07 (2H, m), 2.83 (2H, m), 5.09 (1H, d 6.9 Hz), 5.73 (1H, d <3Hz), 7.39 (2H, m), 7.62 (3H, m), 7.74 (3H , m), 7.95 (4H, m), 8.15 (1H, m), 8.74 (1H, br.s); HRMS (CI+): Calc; 440.998266, Found; 440.997720.



5d: ^{1}H NMR (300 MHz, $CDCl_3$): 1.73 (4H, m), 2.31 (2H, br.m), 2.84 (1H, dd 9.6, 15.0 Hz), 3.66 (1H, dd 3.6, 15.0 Hz), 3.4 0 (1H, br.s), 6.66 (1H, t 3.3 Hz), 7.51 (2H, m), 7.56 (1H, d 8.4 Hz), 7.74 (1H, d 1.8 Hz), 7.90 (1H, dd 2.1, 8.4 Hz), 8.12 (1H, d 2.1 Hz); HRMS (CI+): Calc; 440.998266, Found; 440.998110.



6d: ^{1}H NMR (300 MHz, $CDCl_3$): 1.71 (3H, m), 1.98 (1H, m), 2.17 (1H, m), 2.34 (1H, m), 2.96 (3H, m), 3.17 (1H, br.d 17.4Hz), 3.65 (1H, d 9.0 Hz), 5.24 (1H, d <1.5 Hz), 7.31 (1H, m), 7.54 (2H, m), 7.76 (1H, br.d), 7.81 (1H, d 2.1 Hz), 8.00 (1H, m); HRMS (CI+): Calc; 443.013916, Found; 443. 012405.

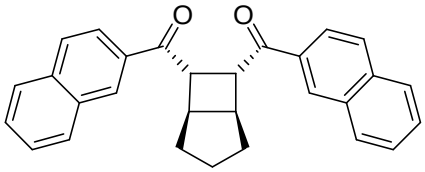


Electrolysis of E,E-1,7-di-1-naphthoyl-1,6-heptadiene (1e)

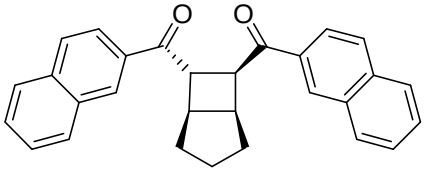
Electrolysis of 97 mg (0.0109 M) of **1e** with Bu_4NBF_4 electrolyte, at –1.8 V (first 3.0 C at –1.5 V). The reaction appeared complete after 4.5 C, or 19.4% (of required charge) had passed through the cell. PTLC purification of the 123 mg of recovered crude yielded *cis*-**2e** (14 mg, 14%), *trans*-**2e** (28 mg, 29%), and **3e** (8 mg, 8%), for a total yield of 50 mg of pericyclic products (51%). No starting material was recovered. A further 16 mg (17%) of **5e** was recovered.

Electrolysis of 104 mg (0.0117 M) of **1e**, with Et_4NBF_4 electrolyte and 25 mg of acetic acid, giving a 1.6:1 excess of acetic acid. Initially at -2.5 V for 15.0 C and then at -3.0 V for 32.0 C. PTLC purification of the crude yielded *trans*-**2e** (6.0 mg, 6%), **5e** (2.8 mg, 3%), **6e** (14.1 mg, 14 %), and **7e** (39.2 mg, 35%).

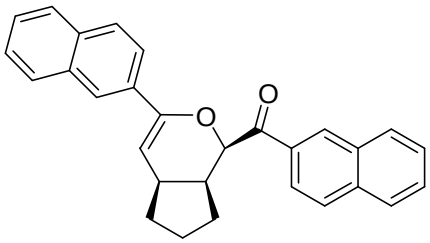
Electrolysis of 98 mg (0.0110 M) of **1e** with Bu_4NBF_4 electrolyte, at -1.5 V. The reaction was stopped after 3.4 C, or 14.5% (of required charge, corrected to 18.4%) had passed through the cell. PTLC purification of the 122 mg of recovered crude yielded *cis*-**2e** (16.6 mg, 21%), *trans*-**2e** (13 mg, 17%), and **3e** (8 mg, 10%), for a total yield of 37.6 mg of pericyclic products (48%). 20.4 mg (21%) of starting material was recovered, along with 5 mg (6%) of **5e**. Reaction is 79% complete based upon recovered **1e.**



cis-**2e**: ^{1}H NMR (300 MHz, $CDCl_3$) 1.74 (2H, m), 1.93 (2H, dd 14.1, 5.4 Hz), 2.15 (2H, m), 3.29 (2H, d 2.4 Hz), 4.08 (2H, d 4.2 Hz), 7.45 (4H, m), 7.74 (4H, m); 7.81 (4H, m), 8.22 (2H, s); HRMS (CI+): Calc; 405.185455; Found 405.185760.

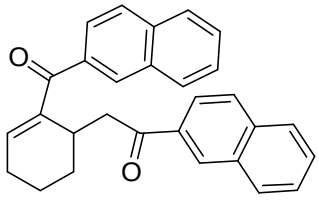


trans-**2e**: ^{1}H NMR (300 MHz, $CDCl_3$): 1.45 (1H, m), 1.62 (1H, m), 1.85 (2H, m), 1.99(2H, m), 3.16 (1H, m), 3.35 (1H, m), 4.50 (1H, m), 4.79 (1H, dd 2.4 Hz, 10.2 Hz), 7.58 (4H, m), 7.89 (4H, m), 8.03 (4H, br.m), 8.48 (1H, br.s), 8.60 (1H, br.s); HRMS (CI+): Calc; 405.185455, Found; 405.186095.

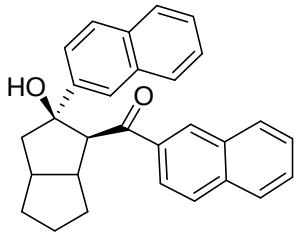


3e: ^{1}H NMR (300 MHz, $CDCl_3$): 1.60 (2H, m), 1.85 (2H, m), 2.07 (2H, m), 2.83 (2H, m), 5.09 (1H, d 6.9 Hz), 5.73 (1H, d <3Hz), 7.39 (2H,

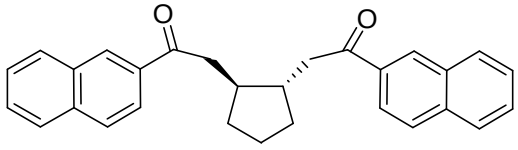
m), 7.62 (3H, m), 7.74 (3H, m), 7.95 (4H, m), 8.15 (1H, m), 8.74 (1H, br.s); HRMS (CI+): Calc; 405.185455, Found; 405.186005.



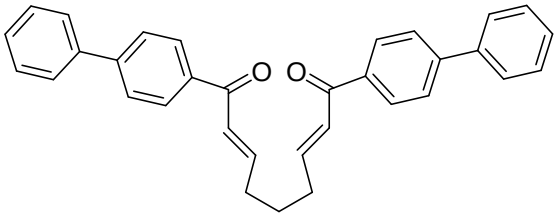
5e[5]: ^{1}H NMR (300 MHz, $CDCl_3$): 1.71 (1H, m), 1.87 (3H, m), 2.35 (2H, br.m), 3.00 (1H, dd 11.4, 15.6 Hz), 3.66 (1H, dd 3.6, 15.6 Hz), 3.77 (1H, br.s), 6.75 (1H, br.t), 7.60 (4H, m), 7.92 (5H, m), 7.99 (1H, m), 8.05 (1H, m), 8.14 (1H, m), 8.22 (1H, s), 8.71 (1H, s).



6e: ^{1}H NMR (300 MHz, $CDCl_3$): Partial only: 1.60 (m), 1.91 (m), 3.20 (2H, m), 5.74 (1H, d 1.8 Hz), 7.41 (2H, m), 7.59 (6H, br.m), 7.76 (2H, m), 7.87 (2H, m), 8.00 (2H, m).



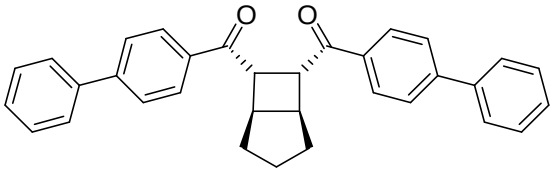
trans-**7e**: ^{1}H NMR (300 MHz, $CDCl_3$): 1.35 (1H, m), 1.67 (2H, m), 1.88 (1H, m), 2.04 (2H, m), 2.31 (1H, m), 2.78 (1H, m), 2.95 (1H, dd 8.1, 15.6 Hz), 3.10 (1H, dd 8.1, 16.2 Hz), 3.27 (1H, dd 5.7, 15.3 Hz), 3.38 (1H, dd 4.8, 16.2 Hz), 7.56 (4H, m), 7.88 (4H, m), 7.95 (2H, br.d 7.8 Hz), 8.02 (2H, m), 8.47 (2H, br.d 6.0 Hz); HRMS (CI+): Calc; 407.201105, Found; 407.202010.



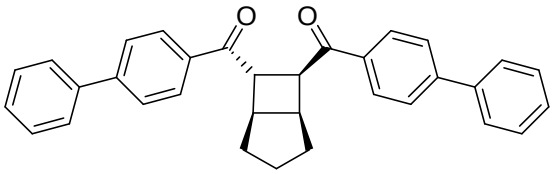
Electrolysis of E,E-1,7-bis(4-phenylbenzoyl)-1,6-heptadiene (1f)

Electrolysis of 76 mg (0.0076M) of **1f** with Bu_4NBF_4 electrolyte (in a 1:1 THF:acetonitrile solution), at -3.5 V (first 1.8 C at -2.5 V, then 1.1 C at -3.0 V). The reaction appeared complete after 11.7 C, or 69.6% (of required charge) had passed through the cell. PTLC purification of the 107 mg of recovered crude yielded *trans*-**2f** (9 mg, 12%). Also recovered was 13 mg (17%) of **5f.**

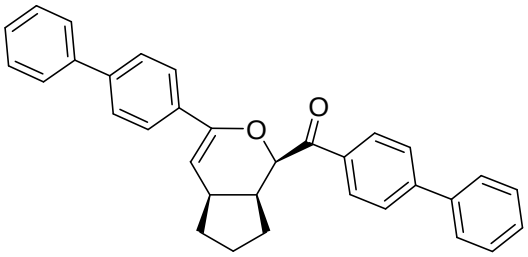
Electrolysis of 55 mg (0.0055M) of **1f** with $Mg(ClO_4)_2$ (0.1 M in 1:1 THF: Acetonitrile) at -2.0 V for 5.0 C (corrected for recovered **1f** to 53.7% of required charge), PTLC purification of the 61 mg of crude yielded *cis*-**2f** (9 mg, 21%), *trans*-**2f** (3.1 mg, 7%), and **3f** (11 mg, 25%), for a total yield of 23.1 mg of pericyclic products (53%). 11mg of unreacted **1f** was recovered, allowing the corrected yields given above. Two additional products were isolated; 5.8 mg (13%) of **6f**; and 3.2 mg (7%) of **7f**.



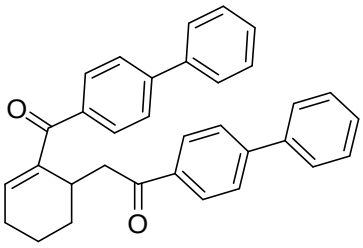
cis-**2f**: ^{1}H NMR (300 MHz, $CDCl_3$): 1.84 (4H, m), 2.06 (2H, m), 3.27 (2H, m), 3.92 (2H, m), 7.37 (6H, m), 7.55 (8H, m), 7.84 (4H, d 8.7 Hz).



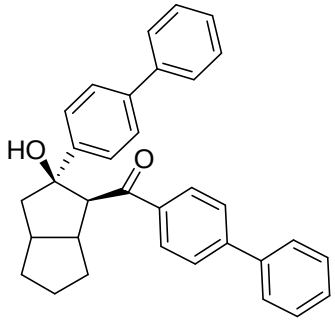
trans-**2f**: ^{1}H NMR (300 MHz, $CDCl_3$): 1.47 (2H, m), 1.66 (2H, m), 1.91 (2H, m), 3.13 (1H, m), 3.30 (1H, m), 4.33 (1H, m), 4.61 (1H, m), 7.45 (6H, m), 7.65 (2H, m), 7.70 (2H, d 8.4 Hz), 8.04 (2H, d 9.0 Hz), 8.11 (2H, d 8.7 Hz); HRMS (CI+): Calc; 457.216755, Found; 457.215380.



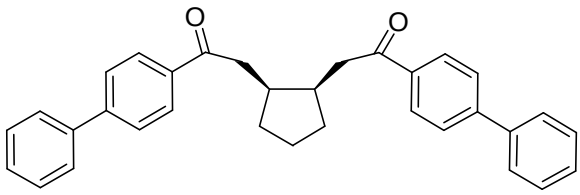
3f: ^{1}H NMR (300 MHz, $CDCl_3$): 1.56 (3H, m), 1.78 (1H, m), 2.05 (2H, m), 2.75 (2H, m), 4.93 (1H, m), 5.61 (1H, m), 7.40-7.72 (12H, m), 8.19 (2H, m). Calc; 457.216755, Found; 457.218026.



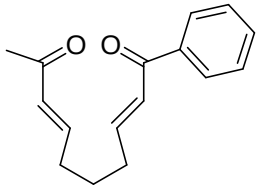
5f: ^{1}H NMR (300 MHz, $CDCl_3$): 1.67 (1H, m), 1.78 (3H, m), 2.31 (2H, br.m), 2.85 (1H, dd 10.5, 14.7 Hz), 3.47 (1H, dd 6.6, 13.8 Hz), 3.54 (1H, br.s), 6.70 (1H, m), 7.43 (6H, m), 7.66 (6H, m), 7.79 (2H, d 8.4 Hz), 8.03 (2H, d 8.7 Hz), 8.16 (2H, d 8.7 Hz); HRMS (CI+): Calc; 457.216755, Found; 457.216312.



6f: ^{1}H NMR (300 MHz, $CDCl_3$): Partial only: 3.94 (1H, d 8.7 Hz), 5.63 (1H, d ~1.5 Hz)



Cis-**7f**: ^{1}H NMR (300 MHz, $CDCl_3$): 1.34 (2H, m), 1.67 (2H, m), 2.02 (2H, m), 2.24 (2H, m), 2.98 (2H, dd 7.2, 17.4 Hz), 3.26 (2H, dd 4.5, 16.2Hz), 7.44 (6H, m), 7.65 (8H, m), 8.03 (4H, d 8.7 Hz); HRMS (CI+): Calc; 459.232406, Found; 459.231734.

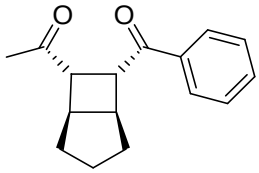


Electrolysis of E,E-1-acetyl-7-benzoyl-1,6-heptadiene (1g)

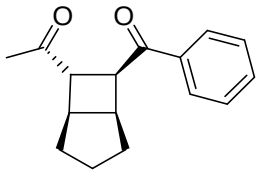
Electrolysis of 98 (0.018M) of **1g** with $Mg(ClO_4)_2$ electrolyte, at -4.5 V for 150 C (initial 4.0 C at -4.0 V, last 16 C at -5.0 V), corresponding to 459% of required charge. PTLC separation yielded *cis*-**2g** (7 mg, 9%), and **7g** (14 mg, 17%), along with 11mg (13%) of an unidentified product, tentatively described as an isomer of **7g** (LRMS (CI+): 245, 227). 16 mg of unreacted **1g** was also recovered

Electrolysis of 73 mg (0.014M) of **1g** with Et_4NBF_4 electrolyte, at -2.0 V for 16.0 C (initial 2.2 C at -1.6 V), corresponding to 55.0% of required charge. PTLC separation

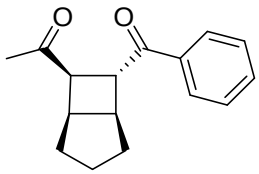
yielded two isomers of *trans*-**2g**, 9 mg (12%) of the isomer where the benzoyl group is *syn* to the cyclopentane ring, and 5 mg (7%) with an *anti* benzoyl group.



cis-**2g**[3]: ^{1}H NMR (300 MHz, $CDCl_3$): 1.59 (2H, m), 1.68 (4H, br.m), 2.03 (3H, s), 3.00 (2H, m), 3.11 (1H, m), 3.79 (1H, dd 4.5, 9.9 Hz), 7.45 (2H, br.t 7.2 Hz), 7.52 (1H, br.t 7.2 Hz), 7.83 (2H, br.d 8.1 Hz); HRMS (CI+): Calc; 243.138505, Found; 243.138743.



trans-**2g (**benzoyl group *syn* to the cyclopentane ring): ^{1}H NMR (300 MHz, $CDCl_3$): 1.36 (2H, m), 1.74 (4H, m), 2.13 (3H, s), 2.93 (1H, m), 3.13 (1H, m), 3.49 (1H, t 8.1 Hz), 4.32 (1H, dd 2.1, 10.5 Hz), 7.47 (2H, br.t 7.2 Hz), 7.57 (1H, br.t 6.9 Hz), 7.93 (1H, br.d 7.2 Hz). X-ray crystallography confirms structure (CCDC 240332)



trans-**2g**[3] **(**benzoyl group *anti* to the cyclopentane ring): ^{1}H NMR (300 MHz, $CDCl_3$): 1.58 (2H, m), 1.80 (4H, m), 2.11 (3H, s), 2.94 (1H, m), 3.07 (1H, m), 3.38 (1H, m), 3.86 (1H, dd 2.4, 10.5 Hz), 3.99 (1H, t 6.3 Hz), 7.45 (2H, br.t 7.2 Hz), 7.55 (1H, br.t 7.2 Hz), 7.95 (1H, br.d 7.2 Hz).

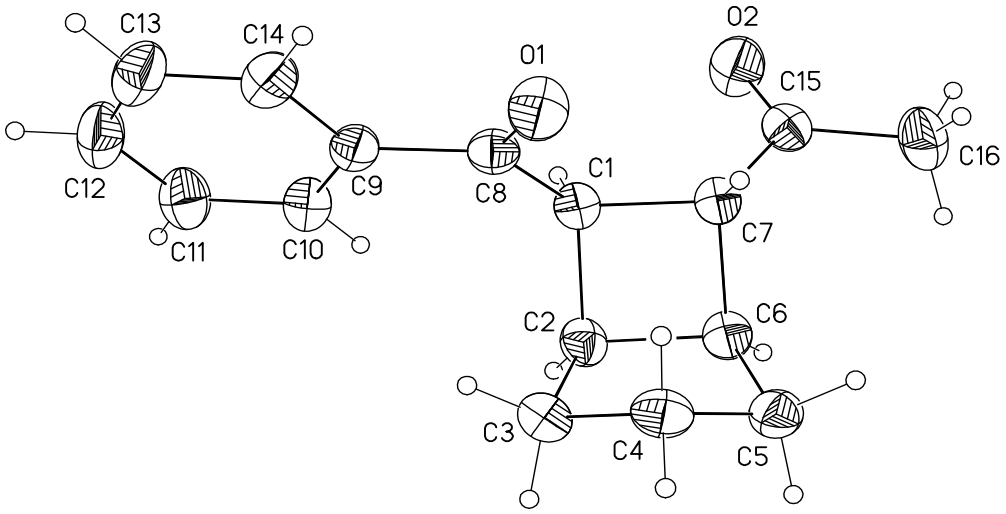
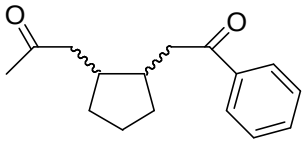
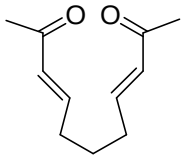


Figure E-6: View of *Tran*-**2g (**benzoyl group *syn* to the cyclopentane ring) showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. CCDC 240332.

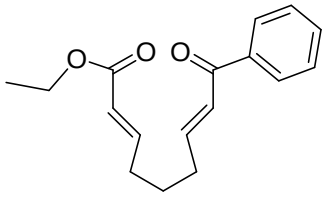


7g: ^{1}H NMR (300 MHz, $CDCl_3$): 1.23 (2H, m), 1.61 (2H, m), 1.98 (4H, br.m), 2.13 (3H, s), 2.40 (1H, dd 7.8, 16.8 Hz), 2.67 (1H, dd 4.2, 16.8 Hz), 2.91 (1H, dd 7.8, 16.5 Hz), 3.14 (1H, dd 4.2, 16.8), 7.46 (2H, br.t 7.5 Hz), 7.56 (1H, br.t 7.2 Hz), 7.95 (1H, br.d 7.2 Hz); HRMS (CI+): Calc; 245.154155, Found; 245.154390.



Electrolysis of E,E-1,7-diacetyl-1,6-heptadiene (1h)

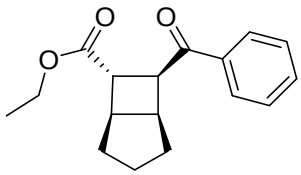
Electrolysis of 97 mg (0.025M) of **1h** with Et_4NBF_4 electrolyte, at -2.5 V for 10.0 C (initial 4.0 C at -2.0 V). ^{1}H NMR (300 MHz, $CDCl_3$) of the 121 mg of recovered crude showed only starting material present (plus electrolyte).



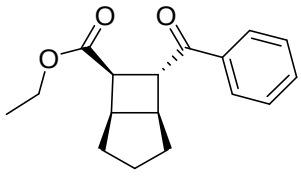
Electrolysis of E,E-7-ethoxy-1-benzoyl-1,6-heptadiene (1i)

Electrolysis of 117 mg (0.020M) of **1i** with $LiClO_4$ electrolyte (0.3M), at -2.0 V for 10.0 C, -2.2 V for 20.0 C, and -3.0 V for 10.0 C (136% of required charge). PTLC separation yielded 23 mg (28%) of one isomer of *trans*-**2i**. Thought to be the same isomer as the major isomer seen in the **1g** electrolysis (based upon NMR comparison). A further 3 mg (4%) of the alternate *trans*-**2i** isomer was also obtained. 34 mg of starting material **1i** was recovered.

Electrolysis of 136 mg (0.023M) of **1i** with Et_4NBF_4 electrolyte, at -2.0 V for 10.5 C. Yielding only unidentified polymers.

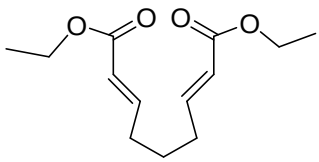


trans-**2i (**benzoyl group *syn* to the cyclopentane ring): ^{1}H NMR (300 MHz, $CDCl_3$): 0.98 (3H, t 7.2 Hz), 1.63 (2H, m), 1.72 (2H, m), 1.91 (2H, m), 3.04 (2H, m), 3.22 (1H, m), 3.69 (1H, dd 5.1, 9.9 Hz), 3.87 (2H, q 7.2 Hz), 7.43 (2H, br.t 8.1 Hz), 7.53 (1H, br.t 6.9 Hz), 7.84 (1H, br.d 7.2 Hz). HRMS (CI+): Calc; 273.149070, Found; 273.148638.



trans-**2i (**benzoyl group *anti* to the cyclopentane ring): ^{1}H NMR (300 MHz, $CDCl_3$): 0.98 (3H, t 7.2 Hz), 1.69 (4H, m), 2.01 (2H, m), 2.99 (1H, m), 3.21

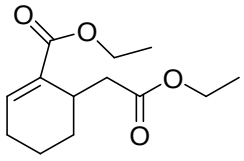
(1H, m), 3.38 (1H, m), 4.14 (2H, q 7.2 Hz), 4.34 (1H, dd 2.7, 10.5 Hz), 7.47 (2H, br.t 6.3 Hz), 7.56 (1H, br.t 6.9 Hz), 7.93 (1H, br.d 6.6 Hz). HRMS (CI+): Calc; 273.149070, Found; 273.148198.



Electrolysis of E,E-1,7-dicarbethoxy-1,6-heptadiene (1j)

Electrolysis of 112 mg (0.021M) of **1j** with Et_4NBF_4 electrolyte, at -2.5 V for 10.0 C, corresponding to 22.2% of required charge. PTLC purification of the 112 mg of recovered crude yielded 47 mg (42%) of **5j.** No starting material was recovered.

Electrolysis of 96 mg (0.018M) of **1j** with $LiClO_4$ electrolyte, at -3.5 V for 4.5 C, -3.5 V for 7.9 C, and -4.0 V for 55 C. ^{1}H NMR (300 MHz, $CDCl_3$) of the recovered crude showed only starting material present.



5j: ^{1}H NMR (500 MHz, $CDCl_3$): 1.26 (3H, t 7.5 Hz), 1.29 (3H, t 7.0 Hz), 1.64 (4H, m), 2.18 (2H, br.m), 2.27 (1H, dd 10.5, 15.0 Hz), 2.64 (1H, dd 3.5, 15.0 Hz), 3.09 (1H, br.s), 4.16 (4H, m), 7.03 (1H, t 4.0 Hz). ^{13}C NMR (500MHz in $CDCl_3$): 14.21 (2C), 17.11, 25.77, 26.52, 29.92, 38.40, 60.20, 60.26, 132.79, 140.99, 166.86, 172.53; NMR COSY (500 MHz) (consistent with structure). HRMS (CI+): Calc; 241.143984, Found; 241.142945.

CHAPTER III

A typical experiment utilizes 60 mg of a given bis(enone) substrate, which equates to 0.16 mmol for substrate **1c**, equating to a typical substrate concentration of 0.0073M. In some cases 100 mg of substrate was used. The electrolyte solution is 0.100M (unless stated) in perchlorate salt, in dry acetonitrile (unless stated). Electrolysis of the substrate was carried out at -2.5 V with stirring under positive nitrogen flow, at room temperature. The applied voltage is in some cases increased (more negative) stepwise, by a few tenths, through the course of an electrolysis to help maintain the current (tracked by coulometer). This was done to allow a reaction to run to completion in a few hours, yet avoid a high initial current that may lead to unwanted oligomerization. The reactant solution (WE compartment only) then underwent an aqueous workup with sequential dichloromethane washings.

Analysis assumes that the recovered crude contains no perchlorate salt, such that the mass of crude (usually within 1 mg of substrate used) contains only products/unreacted substrate. Purification by preparative TLC (1mm thick, elution with ethyl acetate/petroleum ether mixture, 1:9 to 1:4 ratio) had previously been used to allow separation and identification of products (chapter II experimental above). Indeed such purification shows a reasonable correlation between the above assumption and separated yields. While product isomer ratios are accurate, actual yields may be somewhat overestimated. However the product ratios obtained from the crude NMR are thought to be more accurate due to reduction of rounding errors and the chance of disproportionate losses in separation. Two 100 mg sample reactions are looked at below. They clearly show that the crude NMR analysis performed here is sufficient for a study of product

isomer ratios. The estimation of recovered substrate, and extrapolation to percent reaction completion would suggest a slight underestimate of this value. However, maximum percent of charge used is based on this estimation.

	Substrate: **1d**		Substrate:**1f**	
	Mass estimate /mg	Mass obtained /mg	Mass estimate /mg	Mass obtained /mg
trans-**2**	12.9	7	3.0	3.1
cis-**2**	40.2	34	12.3	9
3	22.9	16	15.5	11
4	11.0	6	5.8	5.8
5	-	-	3.8	3.2
Unreacted substrate	-	-	14.6	11

Table E-1: Two examples of the comparison between crude NMR analysis yields to actual PTLC separated yields.

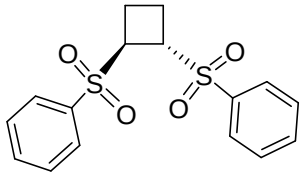
The reference electrode was calibrated for a perchlorate solution. The RE when measured against Cl^- | AgCl | Cl reference electrode using 1.00 M KCl electrolyte gave a potential of +0.070 V. The RE being placed in a 0.100 M $LiClO_4$ acetonitrile solution, connected via a saturated KCl salt bridge. Using the known E^0 for the AgCl reference (+0.2368 V vs. SHE) we get a calibration of +0.307 V for our reference electrode vs. SHE, equivalent to +0.065 V vs. SCE. Given the inherent error and different electrolytes involved it is most reasonable to quote a calibration as +0.1 V vs. SCE.

CHAPTER IV

Electrolyses were carried out at -2.5 V (unless stated), following the general electrolysis procedure, using 0.100 M Et_4NBF_4/acetonitrile electrolyte throughout. Yields and catalytic factors are based upon the limiting reagent, which was varied in each experiment. Novel compounds are characterized by $^1H/^{13}C$ NMR and LRMS/HRMS, and in several cases by x-ray crystallography. Previously observed compounds are only characterized by NMR and referenced appropriately. In the few cases when the limiting reagent was recovered, the yields of products and the catalytic factors are corrected accordingly. In general dichloromethane was used in the workup, due to ease of use and good reagent/product solubility.

Electrolysis of phenyl vinyl sulfone (9b)

Electrolysis of 202 mg (0.055M) of **9b** was carried out for 20.0 C (17.3% of required charge). Upon extraction/PTLC 167 mg (82.7%) of **2bb** was recovered.



2bb:[6] ^1H NMR (300 MHz, $CDCl_3$): 2.35 (2H, m), 2.53 (2H, m), 4.21 (2H, m), 7.53 (4H, m), 7.64 (2H, m), 7.80 (4H, m). LRMS (CI+): 337. X-ray crystallography confirms structure.

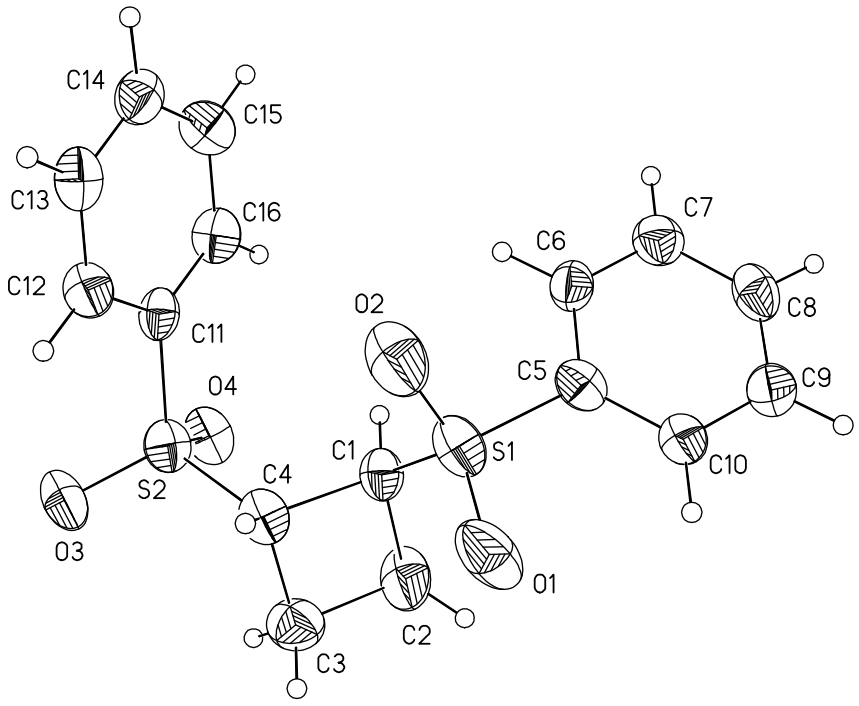
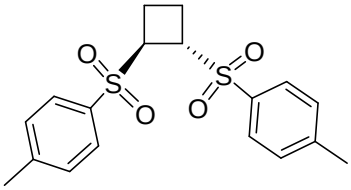


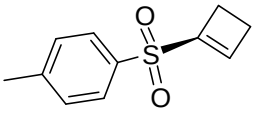
Figure E-7: View of **2bb** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.

Electrolysis of tolyl vinyl sulfone (9c)

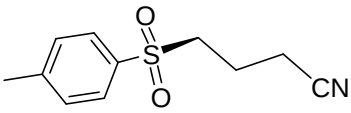
Electrolysis of 157 mg (0.039M) of **9c** was carried out for 23.0 C (31.0% of required charge). Upon extraction/PTLC 98.9 mg (70.6%) of **2cc** was recovered, along with 6.1 mg (3.8%) of **2c-c** (obtained in a mixed band with some **9c**), 7.4 mg (4.3%) of **15c** (obtained in a mixed band with some **2cc**, identified by comparison to **15b**, see chapter six experimental), and 16.1 mg of unreacted **9c**.



2cc:[6] ^{1}H NMR (300 MHz, $CDCl_3$): 2.33-2.52 (4H, m), 2.45 (3H, s), 4.17 (2H, m), 7.29 (4H, d, 8.1 Hz), 7.65 (4H, d, 8.1 Hz).



2c-c:[7] ^{1}H NMR (300 MHz, $CDCl_3$): partial only: 2.51 (2H, td, 1.5, 3.0 Hz), 2.77 (2H, t, 3.0 Hz). Obscured by **9c**, but present by integration: 2.45 (3H, s), 6.64 (1H, t?), 7.35 (2H, d?), 7.79 (2H, d?).



15c: ^{1}H NMR (300 MHz, $CDCl_3$): partial only: 1.81 (2H, m), 3.04 (2H, m), 7.36 (2H, d, 8.7 Hz), 7.75 (2H, d, 8.4 Hz), Obscured by **2cc**, but present by integration: 2.3-2.5 (2H, m), 2.45 (3H, s).

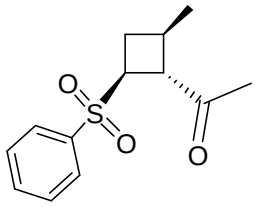
Electrolysis of 9b and 3-penten-2-one (9k)

Electrolysis of 102 mg (85% pure ≡ 86.7 mg, 0.047M) of **9k**, and 103 mg (0.028M) of **9b** (1:1.68 **9b**:**9k**) carried out for 10.1 C (17.4% of required charge). Upon extraction/PTLC 39 mg (25.7%) of **2kb** was recovered, along with 26 mg (25.7%) of **2bb**, ~2 mg (~3%)of **2b-b**, 2 mg of unreacted **9b**, and <1 mg of unreacted **9k**.

Electrolysis of 192 mg (85% pure ≡ 163.2 mg, 0.088M) of **9k**, and 92 mg (0.025M) of **9b** (1:3.53 **9b**:**9k**) carried out for 12.0 C (24.4% of required charge). Upon extraction/PTLC 31 mg (24.1%) of **2kb** was recovered, along with 18 mg (21.0%) of **2bb**, 6.7 mg (13.6%) of **2b-b**, 4 mg (3.7%) of **11kbb**, and 6.3 mg of unreacted **9b**.

Electrolysis, at -2.3 V, of 44 mg (85% pure ≡ 37.4 mg, 0.020M) of **9k**, and 226 mg (0.061M) of **9b** (3.02:1 **9b**:**9k**) carried out for 15.0 C (36.9% of required charge). Upon extraction/PTLC 23.8 mg (22.4%) of **2kb** was recovered, along with 68.4 mg of **2bb**, 4.4 mg of **2b-b**, 28.4 mg of unreacted **9b**, and 2 mg of unreacted **9k**.

Electrolysis of 42 mg (90% pure ≡ 37.8 mg, 0.020M) of **9k**, and 82 mg (0.022M) of **9b** (1.09:1 **9b**:**9k**) carried out for 10.0 C (31.2% of required charge). Upon extraction/PTLC 16.1 mg (19.2%) of **2kb** was recovered, along with 12 mg of **2bb**, 1.9 mg of **2b-b**, 26 mg of unreacted **9b**.



2kb: ^{1}H NMR (300 MHz, $CDCl_3$): 1.28 (3H, d, 6.6 Hz), 2.07 (3H, s), 2.15 (2H, m), 2.33 (1H, m), 3.29 (1H, t, 8.7 Hz), 3.97 (1H, q, 8.7 Hz), 7.55 (2H, m), 7.65 (1H, m), 7.86 (2H, m). X-ray crystallography confirms structure.

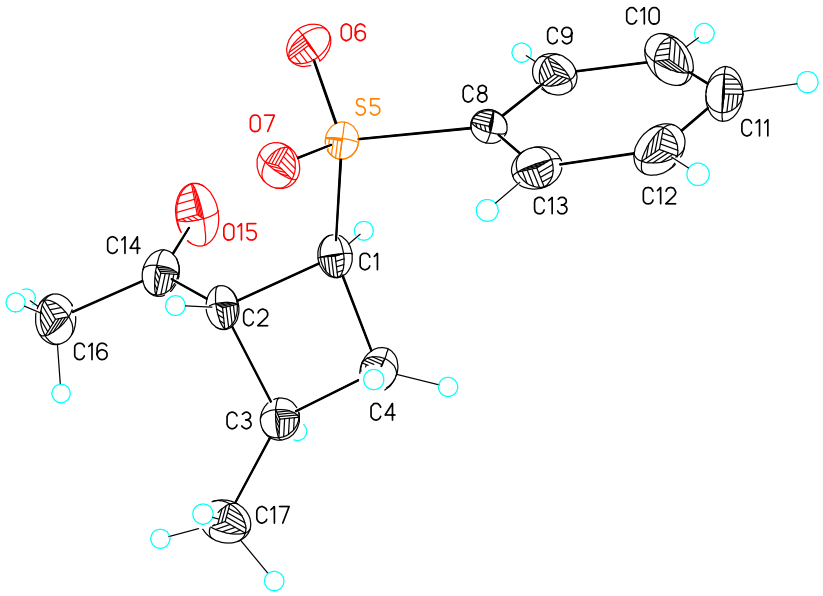
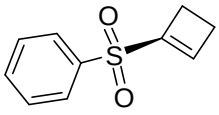
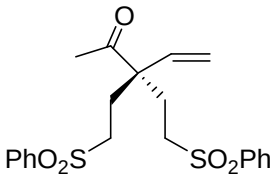


Figure E-8: View of **2kb** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.



2b-b:[7] ^{1}H NMR (300 MHz, $CDCl_3$): 2.52 (2H, td, 1.2, 3.0 Hz), 2.77 (2H, t, 3.0 Hz), 6.67 (1H, t, 1.2 Hz), 7.55 (2H, m), 7.66 (1H, m), 7.79 (2H, m). LRMS (CI+): 195.



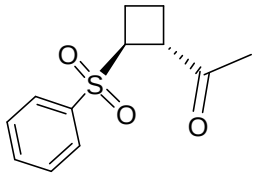
11kbb: ^{1}H NMR (300 MHz, $CDCl_3$): 2.06 (7H, m overlapping s), 2.86 (4H, m), 5.15 (1H, d, 17.7 Hz), 5.37 (1H, d, 10.8 Hz), 5.71 (1H, d, 11.1, 17.7 Hz), 7.60 (4H, m), 7.69 (2H, m), 7.89 (4H, m). LRMS (CI+): 421, 269, 253, 242; HRMS (CI+): Calc.; 421.114203, Found; 421.114343.

Electrolysis of 9b and methyl vinyl ketone (9i)

Electrolysis, at -2.3 V, of 45 mg (0.029M) of **9i**, and 199 mg (0.054M) of **9b** (1.84:1 **9b**:**9i**) carried out for 12.0 C (19.4% of required charge). Upon extraction/PTLC 21.6 mg (14.1%) of **2ib** was recovered, along with 44.4 mg of **2bb**, 3.5 mg of **2b-b**, and 58.5 mg of unreacted **9b**.

Electrolysis, at -2.2 V, of 43 mg (0.028M) of **9i**, and 298 mg (0.081M) of **9b** (2.89:1 **9b**:**9i**) carried out for 12.0 C (20.3% of required charge). Upon extraction/PTLC 41 mg (28.1%) of **2ib** was recovered, along with 64.8 mg of **2bb**, 5.5 mg of **2b-b**, and 106.7 mg of unreacted **9b**.

Electrolysis, at -2.2 V, of 76 mg (0.049M) of **9i**, and 85 mg (0.023M) of **9b** (1:2.14 **9b**:**9i**) carried out for 16.0 C (32.8% of required charge). NMR of crude extract appeared to contain primarily polymeric products, with trace indications of **2ib**, and unreacted **2b**. No further workup.



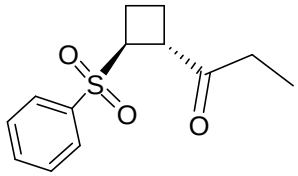
2ib: ^{1}H NMR (300 MHz, $CDCl_3$): 2.08 (3H, s), 2.32 (2H, m), 2.52 (2H, m), 3.76 (1H, ~q, 8.4 Hz), 4.10 (1H, ~q, 8.4 Hz), 7.56 (2H, m), 7.65 (1H, m), 7.87 (2H, m).

Electrolysis of 9b and ethyl vinyl ketone (9j)

Electrolysis, at -2.2 V, of 114 mg (0.062M) of **9j**, and 244 mg (0.066M) of **9b** (1.07:1 **9b**:**9j**) was carried out for 11.8 C (9.0% of required charge). Upon

extraction/PTLC 32.8 mg (9.6%) of **2jb** was recovered, along with 14.7 mg of **2bb**, 9.6 mg of **2b-b**, and 36 mg of unreacted **9b**.

Electrolysis, at -2.2 V, of 35 mg (0.019M) of **9j**, and 203 mg (0.055M) of **9b** (2.90:1 **9b**:**9j**) was carried out for 4.5 C (11.2% of required charge). Upon extraction/PTLC 33.6 mg (32.0%) of **2jb** was recovered, along with 36 mg of **2bb**, 4.7 mg of **2b-b**, and 32.7 mg of unreacted **9b**.



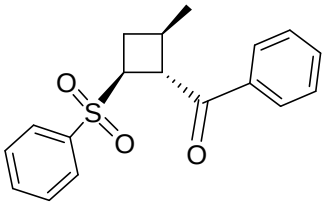
2jb: ^{1}H NMR (300 MHz, $CDCl_3$): 0.98 (3H, t, 7.2 Hz), 2.05 (2H, m), 2.33 (3H, br.m), 2.51 (1H, m), 3.75 (1H, ~q, 8.1 Hz), 4.13 (1H, ~q, 8.1 Hz), 7.56 (2H, m), 7.65 (1H, m), 7.87 (2H, m).

Electrolysis of 9b and phenyl propenyl ketone (9v)

Electrolysis of 176 mg (0.048M) of **9b** and 76 mg (0.024M) of **9v** (2.01:1 **9b**:**9v**) was carried out for 8.0 C (20.9% of required charge). Upon extraction/PTLC 46.4 mg (37.2%) of **2vb** was recovered, along with 18 mg of unreacted **9v**, 43 mg of unreacted **9b**, 4.6 mg of **2b-b**, and a 33 mg impure band with small amounts of **2bb**, but primarily containing the partially characterized trimeric **11vbb**.

Electrolysis of 322 mg (0.087M) of **9b** and 70 mg (0.022M) of **9v** (3.99:1 **9b**:**9v**) was carried out for 23.0 C (58.0% of required charge). Upon extraction/PTLC 57.4 mg (44.5%) of **2vb** was recovered, along with 10 mg of unreacted **9v**, 42.3 mg of unreacted **9b**, 17.3 mg of **2b-b**, and 59 mg impure **2bb**, which contained traces (<2 mg) of the partially characterized trimeric **11vbb**.

Electrolysis of 88 mg (0.024M) of **9b** and 152 mg (0.047M) of **9v** (1.99:1 excess of **9v** over **9b**) was carried out for 25.0 C (24.9% of required charge). NMR of crude extract appeared to contain polymeric products, no indication of any known products (**2bb**, **2vb**, **2b-b**, or **11vbb**), or of unreacted **9b** or **9f**. No further workup.



2vb: ^{1}H NMR (300 MHz, $CDCl_3$): 1.31 (3H, d, 5.7 Hz), 2.33 (3H, m), 4.13 (1H, dd, 7.2, 8.1 Hz), 4.35 (1H, ~q, 8.1 Hz), 7.47 (4H, m), 7.57 (2H, m), 7.85 (4H, m). X-ray crystallography confirms structure.

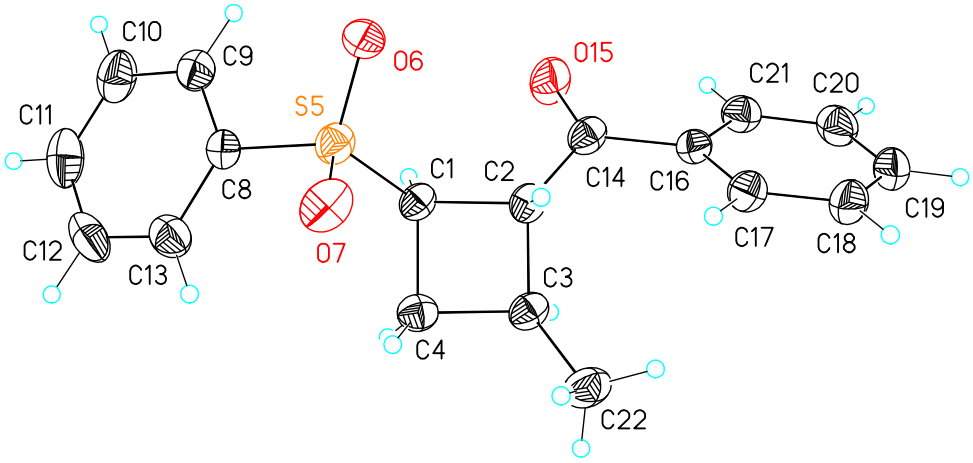
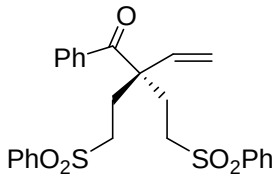


Figure E-9: View of **2vb** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.



11vbb: ^{1}H NMR (300 MHz, $CDCl_3$): partial only: 2.22 (4H, m), 2.80 (2H, m), 2.99 (2H, m), 5.17 (1H, d, 17.7 Hz), 5.40 (1H, d, 10.8 Hz), 5.96 (1H, dd, 10.8, 18.0 Hz).

Electrolysis of 9b and biphenyl vinyl ketone (9w)

Electrolysis, at -2.0 V, of 50 mg (0.010M) of **9w** and 151 mg (0.041M) of **9b** (1:4.00 **9w**:**9b**) was carried out for 3.5 C (17.5% of required charge). Upon extraction/PTLC 22.4 mg (27.7%) of **2wb** was recovered, along with 4 mg of unreacted **9w**, 77.1 mg of unreacted **9b**, 3.5 mg **2bb**, ~5 mg of the trimeric **11wbb**, and 4 mg of **15b** (characterized and discussed in chapter six).

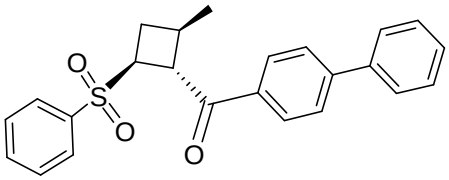
Electrolysis, at -2.0 V, of 51 mg (0.010M) of **9w** and 79 mg (0.021M) of **9b** (1:2.04 **9w**:**9b**) was carried out for 5.4 C (24.4% of required charge). Analysis of the crude product NMR indicated the presence of **11wbb**, while no **2wb** was seen, nor unreacted **9b** or **9w**. 0.36 inches of rainfall.[8]

Electrolysis, at -1.8 V, of 55 mg (0.011M) of **9w** and 85 mg (0.023M) of **9b** (1:2.04 **9w**:**9b**) was carried out for 2.5 C (10.5% of required charge). Analysis of the crude product NMR indicated the presence of **11wbb**, **2wb**, **2bb**, unreacted **9b**, but not **9w**. 0.40 inches of rainfall.[8]

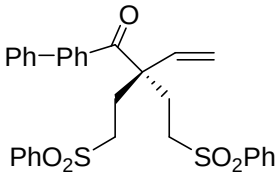
Electrolysis, at -1.8 V, of 60 mg (0.012M) of **9w** and 91 mg (0.025M) of **9b** (1:2.00 **9w**:**9b**) was carried out for 3.5 C (13.4% of required charge). The electrolyte and substrates were placed under vacuum, in glassware fresh from the oven, for five hours

prior to use. Analysis of the crude product NMR indicated the presence of **11wbb**, **2wb**, **2bb**, unreacted **9b**, but not **9w**. No rainfall.[8]

Electrolysis, at -1.6 V, of 40 mg (0.008M) of **9w** and 152 mg (0.041M) of **9b** (1:5.01 **9w**:**9b**) was carried out for 3.3 C (19.0% of required charge). Analysis of the crude product NMR indicated the presence of **11wbb**, **2wb**, **2bb**, unreacted **9b**, but not **9w**. No rainfall.[8]



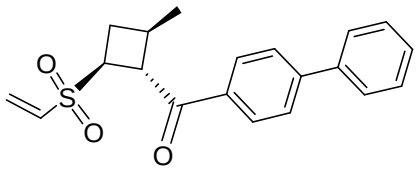
2wb: ^{1}H NMR (300 MHz, $CDCl_3$): 1.34 (3H, d, 6.0 Hz), 2.35 (3H, m), 4.17 (1H, t, 7.5 Hz), 4.35 (1H, q, 8.4 Hz), 7.56 (10H, br.m), 7.90 (4H, m). LRMS (CI+): 391; HRMS (CI+): Calc.; 391.136792, Found; 391.138040.



11wbb: ^{1}H NMR (300 MHz, $CDCl_3$): partial only: 2.22 (4H, m), 2.83 (2H, m), 3.02 (2H, m), 5.18 (1H, d, 17.7 Hz), 5.42 (1H, d, 1 1.1 Hz), 5.99 (1H, d, 10.8, 17.7 Hz).

Electrolysis of divinyl sulfone (9f) and biphenyl vinyl ketone (9w)

Electrolysis, at -2.0 V, of 50 mg (0.010M) of **9w** and 117 mg (0.045M) of **9f** (4.40:1 **9f**:**9w** was carried out for 10.0 C (49.0% of required charge). Upon extraction/PTLC 8 mg (11.1%) of **2wf** was recovered, along with 3 mg of unreacted **9w** and 23 mg of unreacted **9f**.



2wf: ^{1}H NMR (300 MHz, $CDCl_3$): 1.35 (3H, d, 6.0 Hz), 2.27 (1H, m), 2.44 (2H, m), 4.07 (1H, dd, 7.2, 8.1 Hz), 4.35 (1H, ~q, 8.1 Hz), 6.07 (1H, d, 9.3 Hz), 6.39 (1H, d, 16.8 Hz), 6.53 (1H, 9.3, 16.5 Hz), 7.47 (3H, m), 7.63 (2H, d, 7.5 Hz), 7.72 (2H, d, 8.1 Hz), 8.01 (2H, d, 8.4 Hz). LRMS (CI+): 341; HRMS (CI+): Calc.; 341.121142, Found; 341.121053.

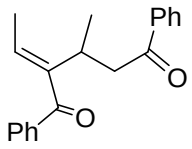
Electrolysis of 9b and ethyl vinyl sulfone (9d) and, 9b and methyl vinyl ketone (9e)

Electrolysis of 59 mg (0.016M) of **9b** and 164 mg (0.062M) of **9d** (3.89:1 **9d**:**9b**) was carried out for 10.0 C (29.6% of required charge). NMR of crude extract shows a small peak at 4.29 (1H? q, 7.8 Hz).

Electrolysis of 81 mg (0.022M) of **9b** and 198 mg (0.085M) of **9e** (3.88:1 **9e**:**9b**) was carried out for 15.0 C (32.3% of required charge). NMR of crude extract shows a small peak at 4.28 (1H? q, 8.1 Hz) and additional singlet peak (0.02 ppm from that of **9e**), LRMS (CI+) of impure band show peaks at 337 (**2bb**) and 275 (**2be**?).

Electrolysis of phenyl propenyl ketone (9v)

Electrolysis, at -2.0 V, of 208 mg (0.064M) of **9v** was carried out for 11.0 C (8.0% of required charge). Upon extraction/PTLC 48 mg (23.1%) of **10vv** was recovered, along with several bands of possible polymers.



10vv: ^{1}H NMR (300 MHz, $CDCl_3$): 1.30 (3H, d, 6.9 Hz), 1.91 (3H, d, 7.2 Hz), 3.32 (1H, m), 3.54 (2H, m), 6.15 (1H, q. 6.9 Hz), 7.42 (6H, m), 7.60 (2H, ~d, 7.2 Hz), 7.94 (2H ~d, 7.2 Hz).). LRMS (CI+): 293; HRMS (CI+): Calc.; 293.154155, Found; 293.154340.

Electrolysis of phenyl vinyl sulfone (9b) in a <0.05M $KClO_4$ electrolyte solution

Electrolysis, at -3.0 V, of 87 mg (0.024M) of **9b** was carried out for 11.6 C (23.2% of required charge). NMR of the 86 mg of crude showed three compounds present in the following ratio: **2bb**:**2b-b**:**2b =** 1:0.57:11.

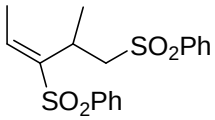
CHAPTER V

All electrolyses were carried out at -2.5 V, following the general electrolysis procedure, using 0.100 M Et_4NBF_4/acetonitrile electrolyte throughout. Yields and catalytic factors are based upon the allyl phenyl sulfone, **8**, limiting reagent. All novel compounds are characterized by $^{1}H/^{13}C$ NMR and LRMS/HRMS, and in several cases by x-ray crystallography (CCDC numbers quoted below). In the few cases when **8** was recovered, the yields of products and the catalytic factors are corrected accordingly. In general dichloromethane was used in the workup, due to ease of use and good reagent/product solubility, exceptions are noted below. Benzene was used on occasion when single products were formed and there were separation problems. Such that PTLC for **11d** and **11e** was not carried out, as NMR/LRMS showed purity, and benzene separation excluded electrolyte. Also these two compounds proved difficult to extract from collected PTLC bands (recovering no **11d** and small amounts of **11e**).

Electrolysis of allyl vinyl sulfone (8)

Electrolysis of 196 mg (0.049M) of **8** was carried out for 9.0 C. Upon extraction/PTLC 156 mg (81.3%) of **10a** was recovered, along with 4mg of unreacted **8** and 4mg (2.1%) of isomeric propenyl vinyl sulfone (**9a**).

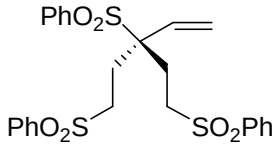
Electrolysis of 188 mg (0.047 M) of **8** and 88 mg (0.024 M; a 1:1.97 ratio relative to **8**) of **9b** was carried out for 3.5 C. NMR analysis of the 296 mg of recovered crude gave a **11b**:**10a** ratio of 1:1.45.



E-4-Methyl-3,5-Bis(phenylsulfonyl)-2-pentene (**10a**)[9]: ^{1}H NMR (300 MHz, $CDCl_3$): 1.21 (3H, d, 6.9 Hz), 1.91 (3H, d, 7.2 Hz), 3.40 (3H, m), 6.95 (1H, q. 7.2 Hz), 7.56 (6H, m.), 7.74 (2H, ~d, 6.9 Hz), 7.83 (2H ~d, 6.9 Hz). An nOe NMR study of **10a** has shown that the methyl group is *trans* to the phenyl sulfonyl group (as shown in Figure V-1), and not *cis* as previously published.[9]

Electrolysis of 8 with phenyl vinyl sulfone (9b)

Electrolysis of 72 mg (0.018M) of **8** and 137 mg (0.037M; a 2.06:1 ratio relative to **8**) of **9b** was carried out for 3.0 C. Upon benzene extraction and PTLC separation, 186 mg (90.8%) of **11b** was recovered, along with 6 mg (<3%) of unidentified product.



E-3,5,7-tris(phenylsulfonyl)-2-pentene (**11b**): ^{1}H NMR (300 MHz in $CDCl_3$): 2.24 (4H, m), 3.05 (2H, m), 3.37 (2H, m), 4.98 (1H, d, 17.4Hz), 5.37 (1H, d, 11.1 Hz), 5.61 (1H, dd, 11.1, 17.1 Hz), 7.49 (2H, m), 7.65 (9H, m), 7.91 (4H, m); LRMS (CI+): 519, 351. X-ray crystallography confirms structure (CCDC 231694).

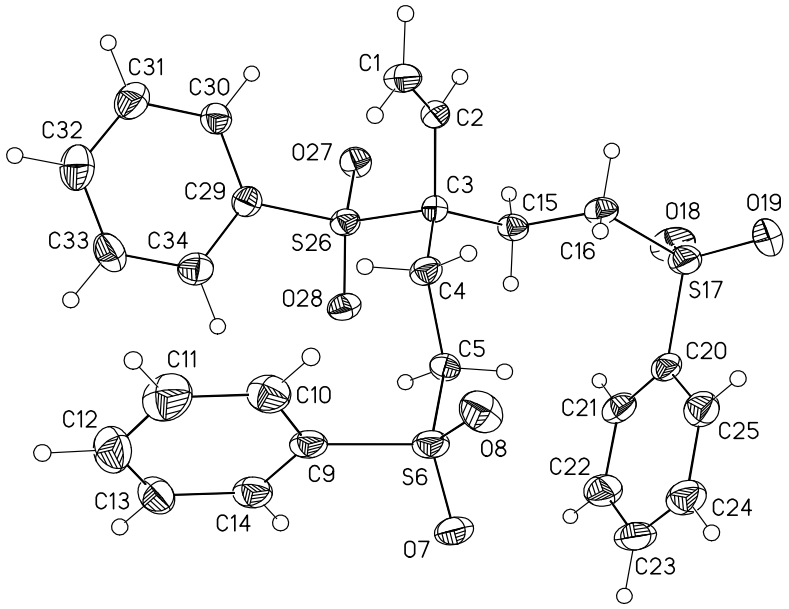
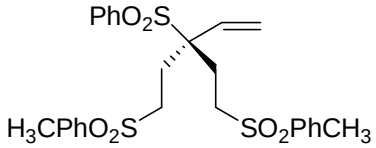


Figure E-10: View of **11b** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. CCDC 231694.

Electrolysis of 8 with tolyl vinyl sulfone (9c)

Electrolysis of 64 mg (0.016M) of **8** and 132 mg (0.033M; 2.06:1 ratio relative to **8**) of **9c** was carried out for 4.6 C. Upon benzene extraction and PTLC separation, 181.5 mg (94.5%) of **11c** was isolated.

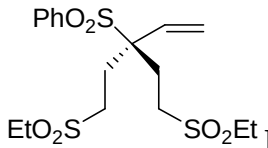


E-3,5,7-tris(4-methylphenylsulfonyl)-2-pentene (**11c**): ^{1}H NMR (300 MHz in $CDCl_3$): 2.22 (4H, m), 2.46 (6H, s), 3.01 (2H, m), 3.31 (2H, m), 4.98 (1H, d, 17.4Hz), 5.37 (1H, d, 11.1 Hz), 5.61 (1H, dd, 11.1, 17.4 Hz), 7.37 (4H, m), 7.45

(2H, t, 7.2 Hz), 7.64 (3H, m), 7.78 (4H, br d, 8.7 Hz); LRMS (CI+): 547, 405; HRMS (CI+): Calc.; 547.128279, Found; 547.128911.

Electrolysis of 8 and ethyl vinyl sulfone (9d)

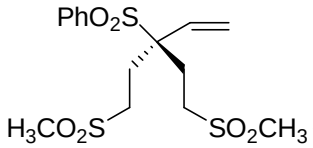
Electrolysis of 99 mg (0.025M) of **8** and 136 mg (0.051M; 2.08:1 ratio relative to **8**) of **9d** was carried out for 3.0 C. Upon benzene extraction, 221 mg (96%) of **11d** was isolated.



E-5,7-bis(ethylsulfonyl)-3-phenylsulfonyl-2-heptene (**11d**): ^{1}H NMR (300 MHz, $CDCl_3$): 1.43 (6H, t, 7.5Hz), 2.30 (2H, m), 2.52 (2H, m), 3.06 (6H, m), 3.33 (2H, m), 5.17 (1H, d, 17.4 Hz), 5.47 (1H, d, 10.8 Hz), 5.75 (1H, dd, 10.8, 17.4 Hz), 7.57 (2H, t, 7.8 Hz), 7.70 (1H, t, 7.5 Hz), 7.81 (2H, d, 8.4 Hz). ^{13}C NMR (300 MHz, $CDCl_3$): 6.9 (2C), 21.6 (2C), 46.2 (2C), 48.2 (2C), 67.9, 122.9, 129.2 (2C), 131.0 (2C), 133.5, 134.0, 134.9. LRMS (CI+): 423, 281. HRMS (CI+): Calc; 423.0970, Found; 423.0960.

Electrolysis of 8 and methyl vinyl sulfone (11e)

Electrolysis of 90 mg (0.022M) of **8** and 108 mg (0.046M; 2.06:1 ratio relative to **8**) of **9e** was carried out for 3.1 C. Upon benzene extraction 178 mg (92%) of **11e** was recovered.



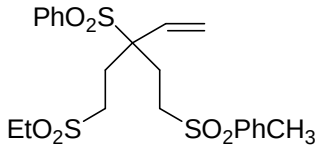
E-5,7-bis(methylsulfonyl)-3-phenylsulfonyl-2-heptene (**11e**): ^{1}H NMR (300 MHz, $CDCl_3$): 2.30 (2H, m), 2.47 (2H, m), 2.99 (6H, s), 3.15 (2H, m), 3.45 (2H, m), 5.16 (1H, d, 17.4Hz), 5.46 (1H, d, 11.1 Hz), 5.76 (1H, dd, 11.1, 17.4 Hz), 7.57 (2H, t, 7.8 Hz), 7.70 (1H, t, 7.5 Hz), 7.81 (2H, d, 8.1 Hz). ^{13}C NMR (300 MHz, $CDCl_3$): 22.1 (2C), 41.4 (2C), 49.1 (2C), 67.9, 123.0, 129.3 (2C), 131.0 (2C), 133.4, 134.0, 135.0. LRMS (CI+): 395, 180. HRMS (CI+): Calc; 395.0657, Found; 395.0662.

Electrolysis of 8 with a mixture of two vinyl sulfone substrates

Electrolysis of 85 mg (0.021M) of **8**, 119 mg (0.032M) of **9b**, and 83 mg (0.031M) of **9d** was carried out for 8.0 C. This amounted to a 1:1.52:1.48 ratio of **8**:**9b**:**9d**. NMR analysis of the 368 mg of recovered crude gave a **11d**:**11bd**:**11b** ratio of 1:3.22:3.42 and a **9d**:**9b** ratio of 17.4:1(no **8**).

Electrolysis of 76 mg (0.019M) of **8**, 114 mg (0.028M) of **9c**, and 76 mg (0.029M) of **9d** was carried out for 8.0 C. This amounted to a 1:1.50:1.52 ratio of **9**:**9c**:**9d**. NMR analysis of the 349 mg of recovered crude gave a **11d**:**11cd**:**11c** ratio of 1:2.80:2.30, and a **9d**:**9c** ratio of 11.7:1 (no **8**).

Electrolysis of 68 mg (0.017M) of **8**, 69 mg (0.017M) of **9c**, and 54 mg (0.020M) of **9d** was carried out for 5.0 C. This amounted to a 1:1.01:1.20 ratio of **9a**:**9c**:**9d**. Upon benzene extraction, NMR analysis of the 206 mg of recovered crude gave a **11d**:**11cd**:**11c** ratio of 1.30:2.00:1, with only **9d** remaining of the three starting materials. PTLC separation gave 32 mg (16%) of **11c** and 62 mg (34%) of **11cd**, along with less than 2mg of **11d** (see above, with reagards to difficulty of **11d** recovery).



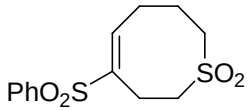
1-ethylsulfonyl,3-phenylsulfonyl,3-ethenyl,5-tolylsulfonyl-pentane (**11cd**): ^{1}H NMR (300 MHz in $CDCl_3$): 1.44 (3H, t. 7.5 Hz), 2.24 (2H, m.), 2.41 (2H, m.), 2.48 (3H, s.), 3.02 (5H, m.), 3.32 (2H, m.), 5.10 (1H, d. 17.7Hz), 5.43 (1H, d. 10.8 Hz), 5.69 (1H, dd. 10.8, 17.4 Hz), 7.40 (2H, d. 8.4 Hz), 7.55 (2H, t. 8.1 Hz), 7.69 (1H, t. 7.5 Hz), 7.77 (4H, m.). ^{13}C NMR (300 MHz, $CDCl_3$): 6.9, 21.6, 21.9, 22.9, 46.2, 48.1, 50.9, 67.8, 122.8, 128.3 (2C), 129.2 (2C), 130.5 (2C), 131.0 (2C), 133.4, 134.0, 134.8, 135.8, 145.6. LRMS (CI+): 485, 343. HRMS (CI+): Calc; 485.1126, Found; 485.1107.

Electrolysis of 79 mg (0.020M) of **8**, 110 mg (0.030M) of **9b**, and 76 mg (0.033M) of **9e** was carried out for 8.0 C. This amounted to a 1:1.51:1.65 ratio of **9a**:**9b**:**9e**. NMR analysis of the 330 mg of recovered crude product gave a **11e**:**11be**:**11b** ratio of 1:2.73:2.69, and a**9e** :**9b** ratio of 6.64:1 (no **8**).

Electrolysis of 88 mg (0.022M) of **8**, 93 mg (0.035M) of **9d**, and 83 mg (0.036M) of **9e** was carried out for 8.0 C. This amounted to a 1:1.62:1.60 ratio of **9a**:**9d**:**9e**. NMR analysis of the 348 mg of recovered crude gave a **9d**:**9c** ratio of 1.36:1 (no **8**), but could not distinguish between the three possible trimers. LRMS analysis of the crude was used to arrive at a **11e**:**11de**:**11d** of 1:2.03:1.15.

Electrolysis of 8 with divinyl Sulfone (9f)

Electrolysis of 90 mg (0.022M) of **8** and 181 mg (0.070M; 3.10:1 ratio relative to **8**) of **9f** was carried out for 6.0 C. Upon extraction/PTLC separation, 48 mg (32.3%) of **12f** was isolated and 19 mg (21.1%) of **8** was recovered. This corresponds to a corrected yield of **12f** of 41.0%.



1-Phenylsulfonyl-5-thia-5,5-dioxycyclohept-1-ene (**12f**): ^{1}H NMR (300 MHz, $CDCl_3$): 2.02 (2H, *p),* 6.6 Hz), 2.60 (2H, m), 2.70 (2H, t, 6.3 Hz), 3.12 (2H, t, 6.3 Hz), 3.22 (2H, t, 5.4 Hz), 7.18 (1H, t, 9.3 Hz), 7.58 (2H, br t, 7.8 Hz), 7.70 (2H, br t, 7.8 Hz), 7.81 (1H, br d, 7.8 Hz); LRMS (CI+): 301. X-ray crystallography confirms structure (CCDC 231693).

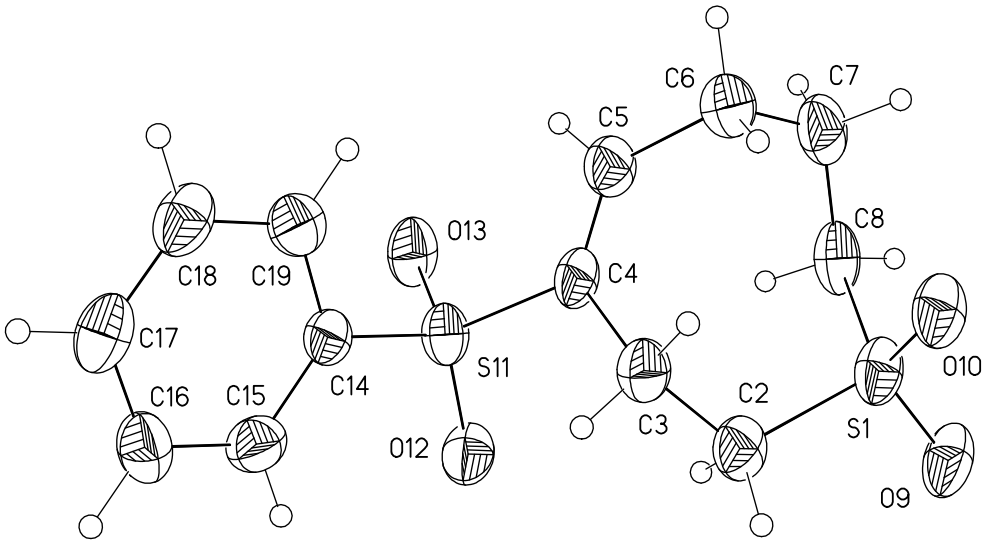
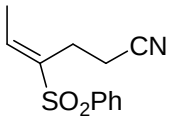


Figure E-11. View of **12f** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. CCDC 231693.

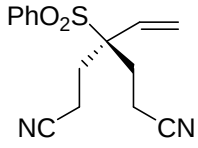
Electrolysis of 8 with acrylonitrile (9g)

Electrolysis of 95 mg (0.024M) of **8** and 57 mg (0.049M; 2.06:1 ratio relative to **8**) of **9g** was carried out for 2.0 C. Upon extraction/PTLC 63 mg (42%) of **11g**, 7 mg (6%) of **10g**, and 3 mg (3%) of **9a** were isolated.

Electrolysis of 80 mg (0.020M) of **8** and 72 mg (0.062M; 3.09:1 ratio relative to **8**) of **9g** was carried out for 3.5 C. Upon extraction/PTLC 72 mg (57%) of **11g** was isolated.



10g: ^{1}H NMR (300 MHz, $CDCl_3$): 1.98 (3H, d, 7.2 Hz), 2.59 (4H, s), 7.18 (1H, q. 7.2 Hz), 7.56 (2H, t, 7.8 Hz), 7.65 (1H, t, 7.8 Hz), 7.86 (2H d, 8.1 Hz). ^{13}C NMR (300 MHz, $CDCl_3$): partial only: 14.8, 22.5, 32.6, 105.9, 128.3 (2C), 129.7 (2C), 133.9, 141.3. LRMS (CI+): 236, 125. HRMS (CI+): Calc.; 236.0745, Found; 236.0747.



11g: ^{1}H NMR (300 MHz, $CDCl_3$): 2.18 (2H, m), 2.36 (2H, m), 2.53 (2H, m), 2.73 (2H, m), 5.14 (1H, d, 17.4 Hz), 5.53 (1H, d, 11.1 Hz), 5.74 (1H, dd, 11.1, 17.4 Hz), 7.60 (2H, t, 7.8 Hz), 7.75 (3H, m). X-ray crystallography confirms structure (CCDC 254787).

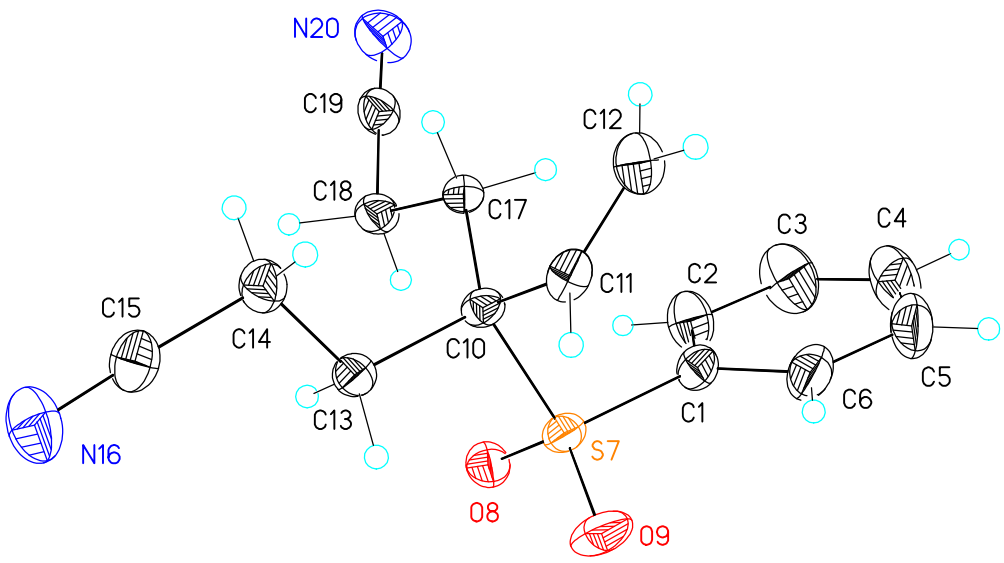
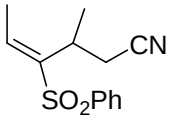


Figure E-12. View of **11g** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. CCDC 254787.

Electrolysis of 8 with crotononitrile (9h)

Electrolysis of 97 mg (0.024M) of **8** and 111 mg (0.075M; 3.11:1 ratio relative to **8**) of **9h** was carried out for 3.3 C. Upon extraction/PTLC 34 mg (26%) of **10h** and 42mg (43%) of **10a** were isolated.

Electrolysis of 89 mg (0.022M) of **8** and 196 mg (0.133M; 5.98:1 ratio relative to **8**) of **9h** was carried out for 4.0 C. Upon extraction/PTLC 26.4 mg (22%) of **10h** and 24.6 mg (28%) of **10a** were isolated.



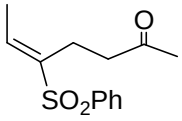
10h: ^{1}H NMR (300 MHz, $CDCl_3$): 1.22 (3H, d, 6.9 Hz), 2.0 1 (3H, d, 7.5 Hz), 2.63 (2H, d, 7.5 Hz) 3.16 (1H, m), 7.11 (1H, q. 7.5 Hz), 7.56 (2H, m), 7.63 (1H, m),

7.86 (2H, m). ^{13}C NMR (300 MHz, $CDCl_3$): 15.0, 18.6, 23.5, 30.7, 118.2, 128.1 (2C), 129.6 (2C), 133.7, 140.4, 140.6, 143.0. LRMS (CI+): 250. HRMS (CI+): Calc.; 250.0902, Found; 250.0904.

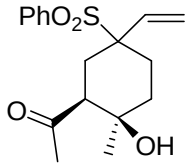
Electrolysis of 8 with methyl vinyl ketone (9i)

Electrolysis of 96 mg (0.024M) of **8** and 37 mg (0.024M; 1.00:1 ratio relative to **8**) of **9i** was carried out for 3.0 C. Upon extraction/PTLC 35.7 mg (28%) of **10i**, 4.1 mg (3%) of **13i** (hydroxyl syn to acetyl), 2.8 mg (2%) of **13i** (hydroxyl anti to acetyl) and 6.3 mg (7%) of **9a** were isolated. 2.7 mg of **8** was recovered.

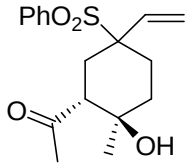
Electrolysis of 86 mg (0.021M) of **8** and 101 mg (0.065M; 3.05:1 ratio relative to **8**) of **9i** was carried out for 4.0 C. Upon extraction/PTLC 21 mg (18%) of **10i**, 11 mg (7%) of **13i** (hydroxyl syn to acetyl) and 7 mg (5%) of **13i** (hydroxyl anti to acetyl) were isolated.



10i: ^{1}H NMR (300 MHz, $CDCl_3$): 1.87 (3H, d, 7.2 Hz), 2.10 (3H, s), 2.44 (2H, t, 7.2 Hz), 2.69 (2H, t, 7.2 Hz), 7.03 (1H, q. 7.2 Hz), 7.53 (2H, m), 7.61 (1H, m), 7.84 (2H, m). ^{13}C NMR (300 MHz, $CDCl_3$): 14.3, 20.3, 30.1, 42.3, 128.2 (2C), 129.5 (2C), 133.5, 138.5, 139.7, 140.9, 207.4. LRMS (CI+): 253, 168, 125. HRMS (CI+): Calc.; 253.0898, Found; 253.0890. An nOe NMR study of **10i** shows methyl group is *trans* to the phenyl sulfonyl group (as shown).



13i (hydroxyl syn to acetyl): ^{1}H NMR (300 MHz, $CDCl_3$): 1.14 (3H, s), 1.25 (1H, m), 1.64 (3H, m), 2.01 (1H, d, 12 Hz), 2.22 (3H, s), 2.45 (3H, m), 3.74 (1H, d, 2.4 Hz), 5.24 (1H, d, 16.8 Hz), 5.64 (2H, m), 7.53 (2H, t, 7.5 Hz), 7.65 (1H, t, 7.8 Hz), 7.80 (2H, d, 7.5 Hz). ^{13}C NMR (500 MHz, $CDCl_3$): 23.8, 27.1, 28.4, 31.1, 34.3, 52.3, 67.4, 68.7, 123.6, 128.5 (2C), 131.0 (2C), 132.8, 133.8, 134.8, 213.8. LRMS (CI+): 323, 305, 181, 163. HRMS (CI+): Calc.; 323.1317, Found; 323.1325. Configuration of the hydroxyl group with regards to the carbonyl group is infered from the NMR shift of the hydroxyl group proton.

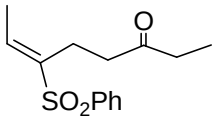


13i (hydroxyl anti to acetyl): ^{1}H NMR (300 MHz, $CDCl_3$): partial only: 1.22 (3H, s), 2.22 (3H, s), 2.84 (1H, s), 5.24 (1H, dd, 1.8, 16.2 Hz), 5.61 (2H, m), 7.52 (2H, m), 7.63 (1H, m), 7.80 (2H, m). ^{13}C NMR (500 MHz, $CDCl_3$): 21.6, 25.7, 28.2, 31.2, 36.8, 54.3, 67.6, 72.1, 123.5, 128.5 (2C), 131.0 (2C), 133.2, 133.9, 134.7, 211.0. LRMS (CI+): 323, 241, 195, 124. HRMS (CI+): Calc.; 323.1317, Found; 323.1312.

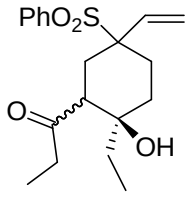
Electrolysis of 8 with ethyl vinyl ketone (9j)

Electrolysis of 95 mg (0.024M) of **8** and 88 mg (0.048M; 2.01:1 ratio relative to **1**) of **9j** was carried out for 7.5 C. Upon extraction/PTLC 37 mg (27%) of **10j** and 1 mg (1%) of **9a** were isolated, along with a trace amount of **13j** (tentatively assigned).

Electrolysis of 93 mg (0.023M) of **8** and 165 mg (0.089M; 3.84:1 ratio relative to **8**) of **9j** was carried out for 6.2 C. Upon extraction/PTLC 64 mg (47%) of **10j** was isolated, along with a trace amount of **13j** (tentatively assigned).



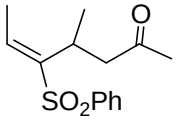
10j: ^{1}H NMR (300 MHz, C DCl_3): 1.03 (3H, t, 7.2 Hz), 1.87 (3H, d, 7.2 Hz), 2.37 (2H, q, 7.2 Hz), 2.45 (2H, t, 7.5 Hz), 2.69 (2H, t, 7.5 Hz), 7.02 (1H, q. 7.2 Hz), 7.53 (2H, m), 7.61 (1H, m), 7.84 (2H m). ^{13}C NMR (300 MHz, $CDCl_3$): 7.9, 14.3, 20.3, 36.1, 40.9, 128.2 (2C), 129.4 (2C), 133.5, 138.5, 139.7, 141.0, 210.1. LRMS (CI+): 267, 209, 191. HRMS (CI+): Calc.; 267.1055, Found; 267.1062.



13j ^{1}H NMR (300 MHz, $CDCl_3$): partial only: 3.73 (1H, d, 2.4 Hz)

Electrolysis of 8 with propenyl methyl ketone (9k)

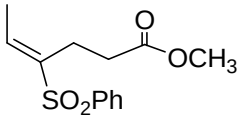
Electrolysis of 100 mg (0.025M) of **8** and 137 mg, corrected to 116 mg (0.063M; 2.52:1 ratio relative to **8**) of **9k** was carried out for 12.6 C. Upon extraction/PTLC 38 mg (26%) of **10k** and 4 mg (4%) of impure **10a** were isolated.



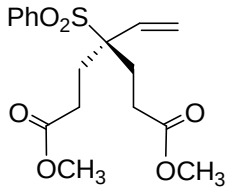
10k: ^{1}H NMR (300 MHz, $CDCl_3$): 1.01 (3H, d, 6.9 Hz), 1.96 (6H, m), 2.68 (2H, m) 3.35 (1H, m), 6.98 (1H, q. 7.2 Hz), 7.51 (2H, m), 7.59 (1H, m), 7.83 (2H, m).). ^{13}C NMR (500 MHz, $CDCl_3$): 14.6, 19.0, 28.1, 30.0, 48.2, 127.9 (2C), 129.1 (2C), 133.1, 138.7, 140.9, 145.1, 206.3. LRMS (CI+): 267, 125. HRMS (CI+): Calc.; 267.1055, Found; 267.1051.

Electrolysis of 8 with methyl acrylate (9l)

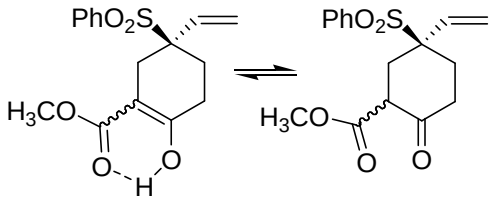
Electrolysis of 85 mg (0.021M) of **8** and 84 mg (0.044M; 2.09:1 ratio relative to **8**) of **9l** was carried out for 18.0 C. Upon extraction/PTLC 22.5 mg (18%) of **10l**, 27 mg (16%) of **11l**, 18.1 mg (12%) of **14l** and 6.4 mg (8%) of **9a** were isolated.



10l: ^{1}H NMR (300 MHz, $CDCl_3$): 1.89 (3H, d, 6.9 Hz), 2.51 (4H, m), 3.65 (3H, s), 7.06 (1H, q. 7.2 Hz), 7.54 (2H, m), 7.62 (1H, m), 7.85 (2H, m). ^{13}C NMR (300 MHz, $CDCl_3$): 14.3, 21.7, 32.9, 52.0, 128.3 (2C), 129.5 (2C), 133.5, 139.0, 139.7, 140.5, 172.9. LRMS (CI+): 269. HRMS (CI+): Calc.; 269.0848, Found; 269.0851.



11l: ^{1}H NMR (300 MHz, $CDCl_3$): 2.12 (2H, m), 2.35 (4H, m), 2.65 (2H, m), 3.69 (6H, s), 5.09 (1H, d, 17.4 Hz), 5.39 (1H, d, 10.8 Hz), 5.75 (1H, dd, 10.8, 17.4 Hz), 7.53 (2H, t, 7.5 Hz), 7.66 (1H, m), 7.80 (2H, m). ^{13}C NMR (300 MHz, $CDCl_3$): 25.0 (2C), 28.7 (2C), 52.2 (2C), 69.0, 121.7, 128.8 (2C), 130.9 (2C), 132.1, 132.6, 134.9, 173.2 (2C). LRMS (CI+): 355, 213. HRMS (CI+): Calc.; 355.1215, Found; 355.1219.



14l: ^{1}H NMR (300 MHz, $CDCl_3$): 1.92-2.02 (1H-keto, m), 2.15-2.51 (4H-enol, 5H-keto, overlapping m), 2.57 (1H-enol, d, 15.9 Hz), 2.86 (1H-enol, d, 15.3 Hz), 3.67 (3H-keto, s), 3.76 (3H-enol, s), 5.10 (1H, d, 17.4 Hz), 5.44 (1H, d, 10.8 Hz), 5.71 (1H, dd, 10.8, 17.4 Hz), 7.55 (2H, t, 7.8 Hz), 7.67 (1H, t, 7.2 Hz),

7.84 (2H, d, 7.8 Hz), 12.08 (1H-enol, s). LRMS (CI+): 323, 181. HRMS (CI+): Calc.; 323.0953, Found; 323.0943. X-ray crystallography confirms enol structure (CCDC 254677).

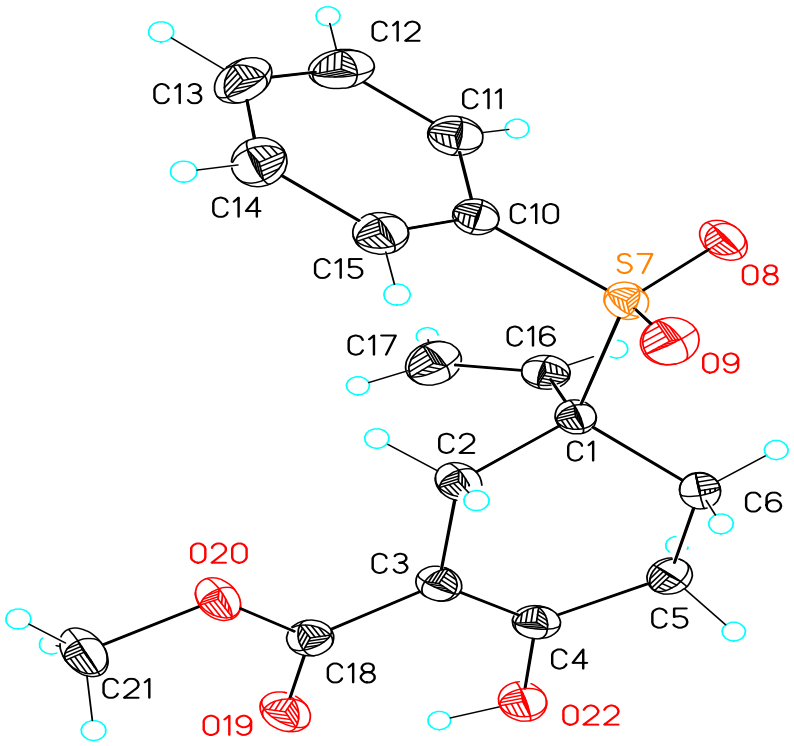
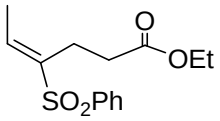


Figure E-13. View of **14l**, enol form, showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. CCDC 254677.

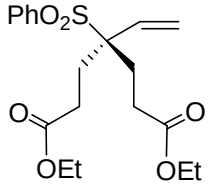
Electrolysis of 8 with ethyl acrylate (9m)

Electrolysis of 87 mg (0.022M) of **8** and 100 mg (0.045M; 2.09:1 ratio relative to **8**) of **9m** was carried out for 9.2 C. Upon extraction/PTLC 34.4 mg (28%) of **10m**, 33.6 mg (20%) of **11m**, 10 mg (7%) of **14m**, 6.6 mg (8%) of **9a** and 2 mg (3%) of **10a** were isolated, along with 8.4 mg of recovered **8**.

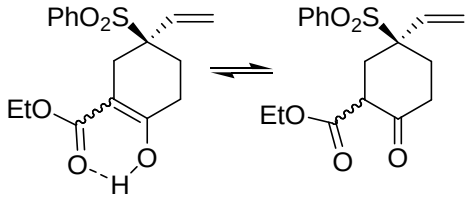
Electrolysis of 84 mg (0.021M) of **8** and 142 mg (0.064M; 3.08:1 ratio relative to **8**) of **9m** was carried out for 22.2 C. Upon extraction/PTLC 16.8 mg (13%) of **10m**, 26.1 mg (15%) of **11m**, 19.8 mg (13%) of **14m**, and 1.3 mg (2%) of **9a** were isolated.



10m: ^{1}H NMR (300 MHz, $CDCl_3$): 1.23 (3H, t, 7.2 Hz), 1.89 (3H, d, 7.2 Hz), 2.49 (4H, m), 4.09 (2H, q, 7.2 Hz), 7.05 (1H, q. 7.2 Hz), 7.53 (2H, m), 7.63 (1H, m), 7.85 (2H, m). ^{13}C NMR (500 MHz, $CDCl_3$): 14.1, 14.2, 21.4, 32.9, 60.6, 128.1 (2C), 129.2 (2C), 133.2, 138.7, 139.6, 140.5, 172.2. LRMS (CI+): 283. HRMS (CI+): Calc.; 283.1004 , Found; 283.1004 .



11m: ^{1}H NMR (300 MHz, $CDCl_3$): 1.26 (6H, t, 7.2 Hz), 2.11 (2H, m), 2.33 (4H, m), 2.63 (2H, m), 4.14 (4H, q, 7.2 Hz), 5.09 (1H, d, 17.7 Hz), 5.38 (1H, d, 10.8 Hz), 5.75 (1H, dd, 10.8, 17.7 Hz), 7.52 (2H, t, 7.5 Hz), 7.65 (1H, m), 7. 80 (2H, d, 7.2 Hz). ^{13}C NMR (500 MHz, $CDCl_3$): 14.2 (2C), 24.8 (2C), 28.7 (2C), 60.8 (2C), 68.9, 121.4, 128.6 (2C), 130.7 (2C), 133.9, 134.8, 135.1, 172.6 (2C). LRMS (CI+): 383, 241. HRMS (CI+): Calc.; 383.1528, Found; 383.1517.

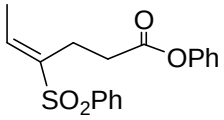


14m: ^{1}H NMR (300 MHz, $CDCl_3$): 1.29 (3H-enol, 3H-keto, overlapping t), 2.14-2.51 (4H-enol, 6H-keto, overlapping m), 2.60 (1H-enol, d, 16.2 Hz), 2.87 (1H-enol, d, 15.6 Hz), 4.22 (2H-keto, 2H-enol, m), 5.10 (1H, d, 17.4 Hz), 5.44 (1H, d, 10.8 Hz), 5.70 (1H, dd, 10.8, 17.4 Hz), 7.55 (2H, t, 7.8 Hz), 7.67 (1H, t, 7.5

Hz), 7.84 (2H, d, 7.2 Hz), 12.16 (1H-enol, s). ^{13}C NMR (500 MHz, $CDCl_3$): 14.2, 24.3, 25.1, 25.7, 60.7, 66.2, 94.3, 122.5, 128.5 (2C), 130.8 (2C), 131.9, 133.9, 135.0, 170.1, 171.7. LRMS (CI+): 337, 195. HRMS (CI+): Calc.; 337.1110, Found; 337.1109.

Electrolysis of 8 with phenyl acrylate (9n)

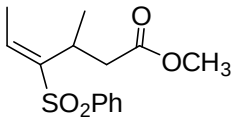
Electrolysis of 110 mg (0.027M) of **8** and 182 mg (0.056M; 2.03:1 ratio relative to **8**) of **9n** was carried out for 35.0 C. Upon extraction/PTLC 40.2 mg (22%) of **10n** and 23.9 mg (24%) of **9a** were isolated, along with 9 mg of recovered **8**.



10n: ^1H NMR (300 MHz, $CDCl_3$): 1.94 (3H, d, 7.2 Hz), 2.65 (2H, m), 2.78 (2H, m), 7.05 (2H, d, 8.4 Hz), 7.12 (1H, q. 6.9 Hz), 7.23 (1H, m), 7.38 (2H, t, 7.8 Hz), 7.55 (2H, m), 7.64 (1H, m), 7.90 (2H m). ^{13}C NMR (300 MHz, $CDCl_3$): 14.5, 21.5, 32.7, 121.7 (2C), 126.1, 126.2, 128.3 (2C), 129.5 (2C), 129.7 (2C), 129.8, 139.4, 140.3, 171.2. LRMS (CI+): 365, 331, 183. HRMS (CI+): Calc.; 331.1004, Found; 331.1012.

Electrolysis of 8 with methyl crotonate (9o)

Electrolysis of 80 mg (0.020M) of **8** and 88 mg (0.040M; 2.00:1 ratio relative to **8**) of **9o** was carried out for 4.0 C. Upon extraction/PTLC 8 mg (6%) of **10o** and 46 mg (58%) of **10a** were isolated.

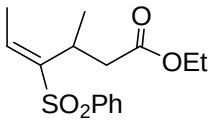


10o: ^1H NMR (300 MHz, $CDCl_3$): 1.10 (3H, d, 7.2 Hz), 1.98 (3H, d, 6.9 Hz), 2.52 (2H, d, 7.8 Hz) 3.29 (1H, q, 7.2), 3.54 (3H, s), 7.06 (1H, q. 7.2 Hz), 7.52 (2H, m), 7.60 (1H, m), 7.85 (2H, m). ^{13}C NMR (500 MHz, $CDCl_3$): 14.6, 18.9 , 29.6,

39.1, 51.6, 128.0 (2C), 129.1 (2C), 133.0, 138.8, 140.7, 144.8, 172.0. LRMS (CI+): 283, 251, 141. HRMS (CI+): Calc.; 283.1004, Found; 283.0995.

Electrolysis of 8 with ethyl crotonate (9p)

Electrolysis of 87 mg (0.022M) of **8** and 114 mg (0.045M; 2.09:1 ratio relative to **8**) of **9p** was carried out for 5.6 C. Upon extraction/PTLC 8 mg (6%) of **10p** and 40 mg (46%) of **10a** were isolated.

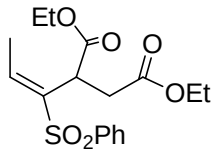


10p: ^{1}H NMR (300 MHz, $CDCl_3$): 1.09 (3H, d, 7.2 Hz), 1.20 (3H, t, 7.2 Hz), 1.98 (3H, d, 7.2 Hz), 2.50 (2H, m) 3.29 (1H, m), 4.00 (2H, q, 7.2 Hz), 7.05 (1H, q. 7.2 Hz), 7.52 (2H, m), 7.60 (1H, m), 7.86 (2H, m). ^{13}C NMR (500 MHz, $CDCl_3$): 14.1, 14.6, 18.9, 29.6, 39.4, 60.5, 128.0 (2C), 129.1 (2C), 133.0, 138.7, 140.7, 144.9, 171.5. LRMS (CI+): 297, 251. HRMS (CI+): Calc.; 297.1161, Found; 297.1158.

Electrolysis of 8 with diethyl maleate (9q), and with diethyl fumarate (9q´)

Electrolysis of 87 mg (0.022M) of **8** and 84 mg (0.022M; 1.02:1 ratio relative to **8**) of **9q** was carried out for 10.0 C. Upon extraction/PTLC 16 mg (11%) of **10q**, 12 mg (16%) of **10a**, and 15.5 mg (20%) of **9a** were isolated, along with 10.5 mg of recovered **8**.

Electrolysis of 99 mg (0.025M) of **8** and 96 mg (0.025M; 1.03:1 ratio relative to **8**) of **9q´** was carried out for 20.0 C. Upon extraction/PTLC 35 mg (22%) of **10q** and 3.6 mg (4%) of **9a** were isolated, along with 18.4 mg of recovered **8**.



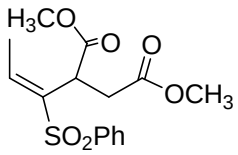
10q: ^{1}H NMR (300 MHz, CDCl $_{3}$): 1.01 (3H, t, 7.2 Hz), 1.23 (3H, t, 7.2 Hz), 1.90 (3H, d, 7.5 Hz), 2.45 (1H, dd, 4.5, 17 .1 Hz), 3.05 (1H, dd, 10.2, 17.1 Hz), 3.91 (2H, m), 4.09 (2H, m), 7.18 (1H, q. 7.2 Hz), 7.53 (2H, m), 7.62 (1H, m), 7.88 (2H, m). ^{13}C NMR (300 MHz, CDCl $_{3}$): 14.1, 14.3, 14.7, 34.8, 39.4, 61.2, 61.7, 128.6 (2C), 129.3 (2C), 133.6, 139.6, 139.7, 141.3, 170.6, 171.3. LRMS (CI+): 355. HRMS (CI+): Calc.; 355.1215, Found; 353.1222.

Electrolysis of 8 with other substrates

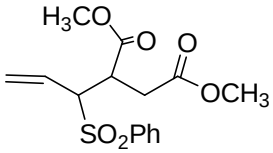
A number of reductions of **8** with a 2-3-fold excess of substrate lead to initial indications of some coupling success. However, in each case problems were encountered during separation, either that crude product mixtures displayed evidence (outlined below) of identifiable products and then upon PTLC separation the evidence was no longer present (say, due to strong adsorption to silica, or further reactivity), or that separation gave rather impure products. Due to time constraints these products were not further purified, as the yields in these cases were rather low (estimated at 10-20%) and not considered sufficiently interesting additions, to this chemical methodology, to warrant additional clarification.

Electrolysis of 63 mg (0.016M) of **8** and 152 mg of **dimethyl maleate**, **9r**, (0.048M, 3.05:1 ratio relative to **8**) was carried out for 12.0 C (36%). Upon extraction/PTLC 25 mg of two impure 1:1 products, 2.50:1 ratio of propenyl:allyl, were obtained, along with an estimated 19 mg of recovered **8**. Small impurities are seen in the 2.4 to 4.2 ppm region, with a large proton methoxy absorbtion at around 3.1 ppm.

Electrolysis of 63 mg (0.016M) of **8** and 152 mg of **dimethyl fumarate**, **9s**, (0.048M, 3.05:1 ratio relative to **8**) was carried out for 12.0 C (36%). Upon extraction/PTLC 25 mg of two impure 1:1 products, 1:3.86 ratio of propenyl:allyl, were obtained, along with an estimated 17 mg of recovered **8**. Impurities are seen in the 2.4 to 4.2 ppm region, with a large proton methoxy absorbtion at around 3.1 ppm.

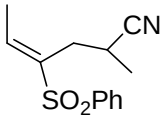


10r (propenyl 1:1): ^{1}H NMR (300 MHz, $CDCl_3$): partial only: 1.91(3H, d, 7.2 Hz), 3.46 (3H, s), 3.64 (3H, s), 7.19 (1H, q, 7. 2 Hz), 7.54 (2H, m), 7.62 (1H, m), 7.86 (2H, m). LRMS (CI+): 327, 295.



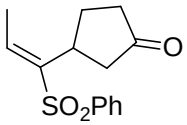
10s (allyl 1:1): ^{1}H NMR (300 MHz, $CDCl_3$): partial only: 4.97 (1H, dd, 5.7, 16.8 Hz), 5.30 (1H, dd, 6.6, 11.1 Hz), 5.82 (1H, m), 7.56 (2H, m), 7.64 (1H, m), 7.85 (2H, m). LRMS (CI+): 327, 295, 291, 259.

Electrolysis of 101 mg (0.025M) of **8** and 77 mg of **methyl acrylonitrile**, **9t**, (0.052M, 2.07:1 ratio relative to **8**) was carried out for 2.50 C (~5%). The crude product displayed ^{1}H NMR peaks for **10a** in approximately a 1.6:1 excess over **10t**.

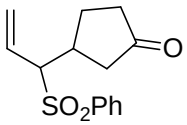


10t ^{1}H NMR (300 MHz, $CDCl_3$): partial only: 1.31 (3H, d, 6.9 Hz), 1.99 (assumed 3H-solvent overlap, d), 2.35 (1H, dd, 6.6, 15.0 Hz), 2.65 (1H, dd, 9.3, 15.0 Hz), 3.11 (1H, m, maybe qd, 2 .7, 7.2 Hz), 7.22 (1H, q, 6.9 Hz), 7.5 -7.9 (assumed 5H-overlap with **10a**).

Electrolysis of 94 mg (0.023M) of **8** and 85 mg of **2-cyclopenten-1-one**, **9u**, (0.047M, 2.01:1 ratio relative to **8**) was carried out for 20.0 C (41%). Upon extraction/PTLC 23 mg of impure product tentatively described as over 50% **10u**, and trace of allyl absorbtion (allyl 1:1 product?), along with 8.1 mg of **9a**, and 2.9 mg of recovered **8**.



10u: ^{1}H NMR (300 MHz, $CDCl_3$): partial only: 7.13 (assumed -1H, q, 7.5 Hz)



10u (allyl?): ^{1}H NMR (300 MHz, $CDCl_3$): partial only: 4.95 (1H, dd, 5.4, 16.8 Hz), 5.28 (1H, dd, 5.4, 10.2 Hz), 5.74 (1H, m).

CHAPTER VI

Cyanomethylation experiments

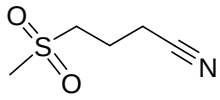
There were problems in the PTLC purification of crude products, obtained from the regular 0.100 M Et_4NBF_4 electrolyte solution and dichloromethane separation, namely that crude products (made up of primary product and electrolyte) would not readily separate. Indeed, PTLC would often give product yields of less than 10%, while an NMR of the crude had suggested much greater yields. Additionally, the water solubility of methyl and ethyl vinyl sulfone was a concern in separation, such that unreacted starting material would not be recovered, and a lower yield calculation would be made. To overcome these combined problems the separations were carried out using benzene and brine (3x150 mL benzene: 20 mL brine), with a 0.010 M Et_4NBF_4 electrolyte solution, and without PTLC. These adaptions to the general procedure were not applied to initial diphenyl sulfone promoted cyanomethylation reactions.

Electrolysis of methyl vinyl sulfone (9e)

Electrolysis, at -3.0 V, of 77 mg (0.033M) of **9e** was carried out for 2.0 C (2.9% of required charge). Upon extraction with 50 mL water/450 mL benzene, 49 mg (45.9%) of **15e** was recovered.

Electrolysis, at -2.7 V, of 104 mg (0.045M) of **9e** was carried out for 3.0 C (3.2% of required charge). Upon extraction with 10 mL brine/450 mL benzene, 133 mg (92.2%) of **15e** was recovered.

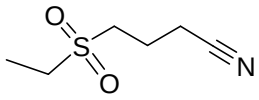
Electrolysis, at -3.0 V, of 84 mg (0.036M) of **9e** was carried out for 2.0 C (2.6% of required charge). Upon extraction with 20 mL brine/450 mL benzene, 109 mg (93.7%) of **15e** was recovered.



15e: ^{1}H NMR (500 MHz, $CDCl_3$): 2.25 (2H, p, 7.0 Hz), 2.66 (2H, t, 7.0 Hz), 2.98 (3H, s), 3.19 (2H, t, 7.0 Hz). ^{13}C NMR (500 MHz, $CDCl_3$): 16.3, 18.5, 52.5, 41.3, 118.2.

Electrolysis of ethyl vinyl sulfone (9d)

Electrolysis, at -3.0 V, of 90 mg (0.034M) of **9d** was carried out for 2.0 C (2.8% of required charge). Upon extraction with 20 mL brine/450 mL benzene, 116 mg (96.2%) of **15d** was recovered.

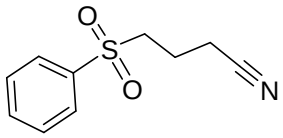


15d: ^{1}H NMR (300 MHz, $CDCl_3$): 1.42 (3H, t, 7.5 Hz), 2.24 (2H, p, 7.2 Hz), 2.66 (2H, t, 7.2 Hz), 3.01 (4H, overlapping t and q).

Electrolysis of diphenyl sulfone (DS), with addition of phenyl vinyl sulfone (2b)

Electrolysis, at -3.0 V, of 88 mg (0.018M) of **DS** was carried out for 8.0 C (20.5% of required charge). With no further charge, 68 mg (0.018M) of **9b** (**9b**:**DS** = 1:1.00) was added, and stirred for ten minutes. Upon extraction/PTLC 23 mg (31.3%) of **15b** along with 9 mg of recovered **9b** and 45 mg of recovered **DS**.

Electrolysis, at -2.2 V, of 74 mg (0.020M) of **9b** and 50 mg (0.010M) of **DS** (**9b**:**DS** = 1:0.50) was carried out for 5.4 C (12.7% of required charge). NMR of crude extract showed primarily **2bb**, with trace unreacted **9b**.



15b: ^{1}H NMR (300 MHz, $CDCl_3$): 2.16 (2H, p, 7.2 Hz), 2.61 (2H, t, 7.2 Hz), 3.24 (2H, t, 7.2 Hz), 7.65 (2H, m), 7.72 (1H, m), 7.94 (2H, m).

Electrolysis of 8 with phenyl acrylate (9n) and diphenyl sulfone (DS)

Electrolysis of 76 mg (0.019M) of **8**, 133 mg (0.041M) of **9n**, 50 mg (0.010M) of **DS** (**8**:**9n**:**DS** = 1:2.15:0.55) was carried out for 10.0 C. Upon extraction/PTLC 43.6 mg (34%) of **10n** and 12.5 mg (18%) of **9a** were isolated, along with 5.1 mg of recovered **8**, 35.8 mg of recovered **DS**, and 17 mg of recovered **9n**.

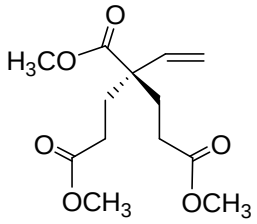
Electrolysis of 8 with methyl acrylate (9l) and DS

Electrolysis of 108 mg (0.027M) of **8**, 115 mg (0.061M) of **9l**, 65 mg (0.014M) of **DS** (**8**:**9n**:**DS** = 1:2.25:0.50) was carried out for 10.0 C. Upon extraction/PTLC 17.4 mg (13%) of **10l**, 12.5 mg (7%) of **11l**, 8.1 mg (5%) of **14l** and 6.9 mg (8%) of **9a** were isolated, along with 16.2 mg of recovered **8**, and 57.5 mg of recovered **DS**. The PTLC separation did not give particularly good separation, such that several bands contained three to five products, such that NMR integration of unique peaks was used to detemine these yields.

Electrolysis of methyl crotonate (9o) with methyl acrylate (9l) and DS

Electrolysis of 64 mg (0.029M) of **9o**, 120 mg (0.063M) of **9l**, 70 mg (0.015M) of **DS** (**8**:**9n**:**DS** = 1:2.18:0.50) was carried out for 5.0 C (8.1% of required charge). Upon

extraction/PTLC 14.3 mg (7.8%) of **11oll** was isolated along with 64 mg of recovered **DS**.



11oll: ^{1}H NMR (300 MHz, $CDCl_3$): 2.05 (4H, m), 2.28 (4H, m), 3.66 (6H, s), 3.71 (3H, s), 5.16 (1H, d, 17.7 Hz), 5.27 (1H, d, 11.1 Hz), 5.95 (1H, q, 11.1, 17.7 Hz).

Electrolysis of phenyl vinyl sulfone (9b) with 3-penten-2-one (9k), and additives

Electrolysis, at -2.2 V, of 44 mg (85% pure ≡ 34.9 mg, 0.019M) of **9k**, 212 mg (0.057M) of **9b**, 8 mg (0.004M) of **phenol** (**9k**:**9b**:**phenol** = 1:3.04:0.21) was carried out for 10.0 C (25% of required charge). Upon extraction/PTLC 37.6 mg (21.6%) of **11kbb** was isolated along with ~3 mg (~3%) of **2kb**, <1mg of **2b-b** (yet no **2bb**) and 35 mg of recovered **9b**.

Electrolysis, at -2.0 V, of 44 mg (90% pure ≡ 39.6 mg 0.021M) of **9k**, 89 mg (0.024M) of **9b**, 33 mg (0.025M) of **acetic acid** (**9k**:**9b**:**acetic acid** = 1:1.10:1.14) was carried out for 31.0 C (67.2% of required charge). NMR of the crude extract showed only **9b**, along with some minor impurities.

Electrolysis of 55 mg (90% pure ≡ 49.5 mg, 0.027M) of **9k**, 206 mg (0.056M) of **9b**, 39 mg (0.008M) of **DS** (**9k**:**9b**:**DS** = 1:2.08:0.30) was carried out for 15.0 C (26.4% of required charge). NMR of crude extract gave regular mix of **2kb**, **2bb**, **2b-b**, and unreacted **9b**, no **11kbb**.

Electrolysis of allyl phenyl sulfone(8), with acid, and with phenyl vinyl sulfone (9b)

Electrolysis of 116 mg (0.029M) of **8**, and 42 mg (0.029M) of **Malononitrile** (**8**:**Malononitrile** = 1:1.00) was carried out for 30.7 C (50% of required charge). NMR of crude extract showed no reaction, just unreacted **8**.

Electrolysis of 103 mg (0.026M) of **8**, and 27 mg (0.013M) of **Phenol** (**8**:**Phenol** = 1:0.51) was carried out for 54.5 C (100% of required charge). NMR of crude extract showed no coupling reaction, just isomerization, unreacted **8**:**9a** = 1:3.41.

Electrolysis of 107 mg (0.027M) of **8**, and 582 mg (1.3M) of $\mathbf{D_2O}$ (**8**: $\mathbf{D_2O}$ = 1:50) was carried out for 20.0 C (35.3% of required charge). NMR of crude extract showed no coupling reaction, just isomerization, unreacted **8**:**9a** = 1:2.89, and some minor impurities.

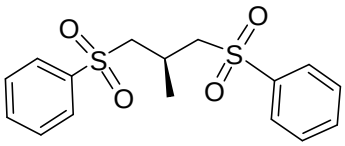
Electrolysis of 83 mg (0.021M) of **8**, and 247 mg (0.62M) of $\mathbf{H_2O}$ (**8**: $\mathbf{H_2O}$ = 1:30) was carried out for 43.9 C (100% of required charge). Upon extraction/PTLC 12 mg (14.5%) of **10a** was isolated along with 15 mg (19.5%) of **16a**, and 8 mg (11.3%) of methyl phenyl sulfone.

Electrolysis of 80 mg (0.020M) of **8**, 160 mg (0.043M) of **9b**, 29 mg (0.022M) of **Acetic acid** (**8**:**9b**:**Acetic acid** = 1:2.17:1.10) was carried out for 35.0 C (82.5% of required charge). NMR of crude extract showed no reaction, just unreacted **8** and **9b**.

Electrolysis of 80 mg (0.020M) of **8**, 159 mg (0.043M) of **9b**, 44 mg (0.022M) of **Phenol** (**8**:**9b**:**Phenol** = 1:2.15:1.06) was carried out for 42.3 C (100% of required charge). NMR of crude extract showed no coupling reaction, just isomerization, unreacted **8**:**9a** = 1:3.82, along with a little **2bb** and unreacted **9b**.

Electrolysis of 85 mg (0.021M) of **8**, 167 mg (0.045M) of **9b**, 24 mg (0.024M) of **Ethanol** (**8**:**9b**:**Ethanol** = 1:2.13:1.12) was carried out for 3.6 C (8.0% of required charge). NMR of crude extract showed regular reaction, single product **11b**, and a little unreacted **8**.

Electrolysis of 91 mg (0.023M) of **8**, 176 mg (0.048M) of **9b**, 54 mg (0.12M) of **D_2O** (**8**:**9b**:**D_2O** = 1:2.04:5.41) was carried out for 3.5 C (7.3% of required charge). NMR of crude extract showed regular reaction, single product **11b**, and a little unreacted **8**.



16a: ^{1}H NMR (300 MHz, $CDCl_3$): 1.32 (3H, d, 6.9 Hz), 2.62 (1H, m), 3.08 (2H, dd, 6.0, 14.4 Hz), 3.54 (2H, dd, 6.3, 14.4 Hz), 7.58 (2H, m), 7.68 (1H, m), 7.87 (2H, m). LRMS (CI+): 339.

Attempts at isomerization

Electrolysis of 104 mg (0.026M) of **8**, and 16 mg (0.007M) of **Phenol** (**8**:**Phenol** = 1:0.30) was carried out for 55.1 C (100% of required charge). NMR of crude extract showed **10a**, **9a** and unreacted **8**, (1:1.94:0.42, respectively).

Electrolysis of 254 mg (0.063M) of **8**, and 65 mg (0.031M) of **Phenol** (**8**:**Phenol** = 1:0.50) was carried out for 48.8 C (36.3% of required charge). NMR of crude extract showed **9a** and unreacted **8** (3.20:1), along with 15 mg (5.9%) of an unidentified coupling product (from PTLC): ^{1}H NMR (300 MHz, $CDCl_3$): 2.51 (3H, m), 3.22 (2H, dd, 5.7, 14.4 Hz), 3.48 (2H, dd, 6.3, 14.4 Hz), 5.06 (2H, overlapping d, 10.5 and 21.3? Hz), 5.48 (1H, m), 7.58 (2H, m), 7.68 (1H, m), 7.85 (2H, m). LRMS (CI+): 365.

Electrolysis of 108 mg (0.022M) of **DS** was carried out for 5.0 C (12% of required charge). 80 mg (0.020M) of **8** was then added without additional current flow (**8**:**DS** = 1:1.13), stirred for ten minutes. NMR of crude extract showed **10a**, and trace amounts of **9a**.

Electrolysis of 35 mg (0.008M) of **Benzil** was carried out for 5.0 C (11% of required charge). 89 mg (0.022M) of **8** was then added without additional current flow (**8**:**DS** = 1:1.13), stirred for ten minutes. NMR of crude extract showed **9a** and **8** (2.54:1).

Electrolysis of 120 mg (0.036M) of **Allyl phenyl sulfide** was carried out for 65.0 C (84.3% of required charge). Upon extraction/PTLC 40 mg (33.3%) of **Propenyl phenyl sulfide** was isolated, although the crude product NMR suggested no other compounds were present (other than electrolyte). ^{1}H NMR (300 MHz, $CDCl_3$): 1.83 (3H, dd, ~0.9, 6.9 Hz), 5.86-6.23 (2H, br. m), 7.16-7.36 (5H, m).

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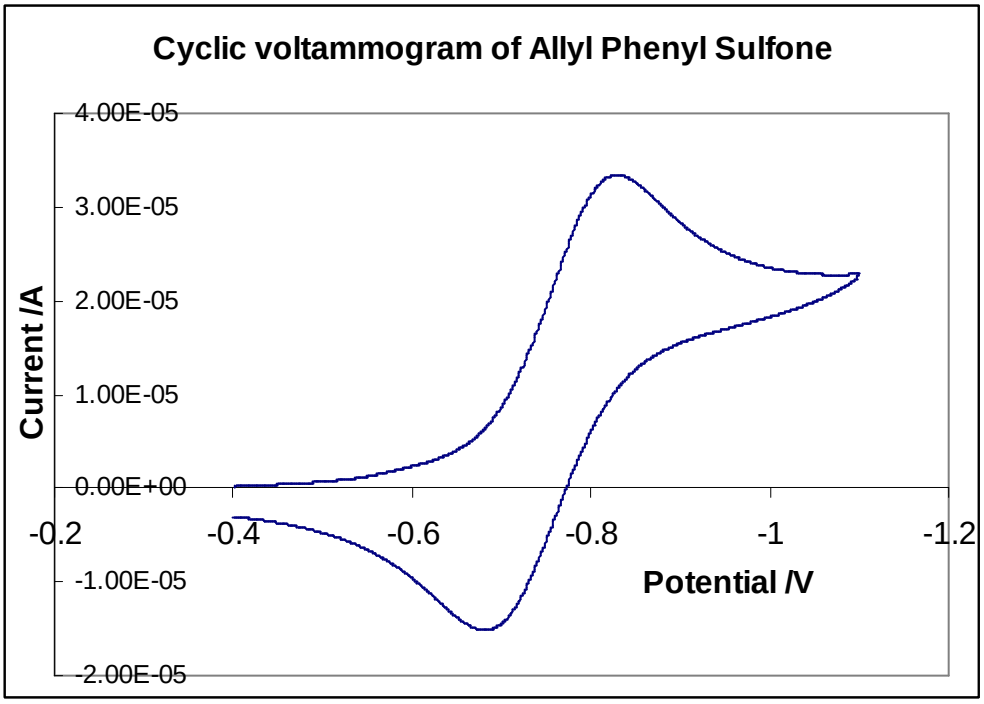
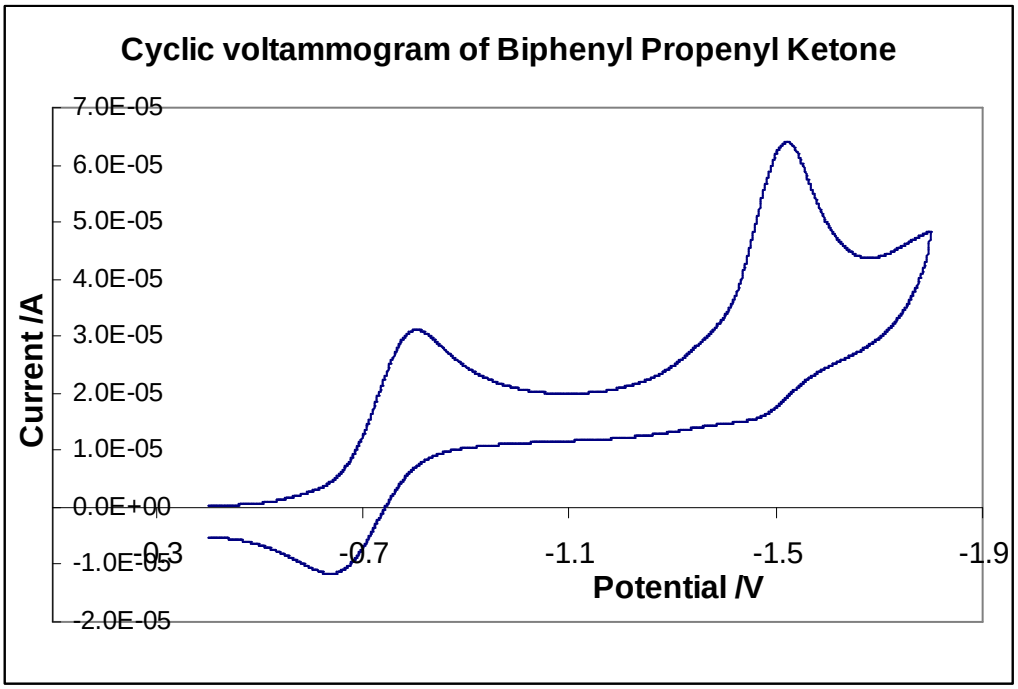
APPENDIX 1: Reduction potentials

Cyclic voltammetry work was carried out using a CH Instruments 700A Electrochemical Analyzer at a scan rate of 0.10 V/s, and at $1x10^{-5}$ sensitivity. The working electrode was glassy carbon (not RVC), with a sliver mesh counter electrode and silver wire reference electrode. The quiescent dry acetonitrile solution was 0.100 M in Et_4NBF_4. Solutions were degassed ~5 minutes. Subtrate concentrations were 6-21 mmol. Ferrocene was used as an internal standard, to reference below potentials to SCE. Potentials given in parenthesis were those obtained in duplicate runs, indicating degree of error in stated numbers, such that potentials are given to 0.01. In most cases cyclic voltametry was just used to track the first reduction potential, although in some second (and third) reductions are given. Below are two sample cyclic voltammograms, followed by tabulated peak current reduction potentials (E_p^-) and peak current (reverse wave) oxidation potentials (E_p^+) for a variety of compounds.





Compound	E_p^- Reduction Potential /V	E_p^+ Reverse Oxidation Potential /V
Phenyl vinyl sulfone	-1.13	-0.96
Methyl vinyl sulfone	-0.89	-0.74
Diphenyl sulfone	-0.86	-0.71
Allyl phenyl sulfone	-0.83	-0.68
Phenyl methyl sulfone	-0.82	-0.67
Trans-Styrl phenyl sulfone	-0.77, -1.62, -2.13	-0.68
Divinyl sulfone	-0.81	-0.64
Methyl vinyl ketone	-0.824 (-0.817)	-0.674 (-0.672)
Ethyl vinyl ketone	-0.80	-0.67
Methyl propenyl ketone	-0.96	-0.83
Phenyl propenyl ketone	-0.907, -1.66 (-0.888)	-0.713 (-0.693)
Biphenyl propenyl ketone	-0.80, -1.52	-0.64
4-vinylpyridine	-0.86	-0.70
Acrylonitrile	-0.82	-0.65
Crotononitrile	-0.82	-0.67
Benzil	-1.04	-0.71
Phenyl acrylate	-1.19, -2.34	-1.05
Ethyl acrylate	-0.81, -2.12	-0.69
Ethyl crotonate	-0.86, -2.38	-0.74
Dimethyl fumarate	-0.80	-0.67

VITA

Greg Andrew Nicholas Felton was born in Basildon, Essex, England on January 9th 1979, the son of Shelagh Carol Felton and George Felton. Upon completion of schooling, at Chalvedon school and sixth form college, Pitsea, Essex, in 1997, he attended The University of Leicester, England. He spent a year (1998-99) as an undergraduate exchange student/summer researcher at Colorado State University, in Fort Collins, CO. He received a Bachelor of Science (Hons.) from The University of Leicester in 2000. He entered the Chemistry and Biochemistry department of the University of Texas at Austin in 2000. During that time he has held a variety of teaching assistant positions, including a senior TA/lecturer position, for which he received the UT Austin Faraday Teaching excellence award in 2003.

The following is a current list of my publications, as of April 2005:

1. "Efficient electrocatalytic addition reactions of allyl phenyl sulfone to electron deficient alkenes" Felton, G. A. N.; Bauld, N. L. *Tetrahedron* **2005**, *61*(14), 3515-3523
2. "Efficient electrocatalytic intramolecular anion radical cyclobutanation reactions" Felton, G. A. N.; Bauld, N. L. *Tetrahedron* **2004**, *60*(48),1099 9-11010.
3. "Dramatic effects of the electrolyte cation on the selectivity of electroreductive cycloaddition reactions of bis(enones)" Felton, G.A.N.; Bauld, N.L. *Tetrahedron Lett.* **2004**, *45*(46), 8465 -8469.
4. "Highly efficient, catalytic bis addition reactions of allyl phenyl sulfone to vinyl sulfones" Felton, G.A.N.; Bauld, N.L. *Tetrahedron Lett.* **2004**, *45*(25), 4841 -4845.
5. "Chemically induced anion radical cycloadditions: intramolecular cyclobutanation of bis(enones) via homogeneous electron transfer," Yang, J.; Felton, G. A. N.; Bauld, N. L.; Krische, M. J. *J. Am. Chem. Soc.* **2004**, *126*, 1634-1635.
6. "An investigation into the enzymatic and kinetic properties of cytosolic soybean ascorbate peroxidase" Undergraduate honours dissertation, spring **2000**.
7. "Electrocatalytic intermolecular anion radical cyclobutanation reactions" Felton, G. A. N.; Bauld, N. L. (In preparation, *Org. Lett.* **2005**).

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